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WORLD HEALTH ORGANIZATION

In this issue

- *An apparent increase in the incidence of juvenile delinquency is causing serious anxiety in many parts of the world. The possible causes of this anxiety, the factors encouraging juvenile delinquency today, and the preventive treatment of potential delinquents are among the questions discussed in a new WHO publication (see page 39).*

- *Irrigation schemes in Africa are proving a mixed blessing. While promoting economic development, they can also—unless suitable precautions are taken —spread disease by multiplying the number of breeding-places for the snail vectors of bilharziasis (see page 59).*

- *The use of the oral antibiotic griseofulvin may revolutionize the treatment of many of the dermatomycoses. Its superiority over fungicidal ointments or X-rays in the mass treatment of ringworm of the scalp has been demonstrated in a recent trial in Israel (see page 64).*

- *Last July, WHO was asked by the Secretary-General of the United Nations to help the Government of the newly independent Republic of the Congo (Leopoldville) avert a total breakdown of the country's health services. This operation has involved not only steps to deal with the immediate emergency but also long-term measures to ensure efficient national health services in the future (see page 45).*

- *Over 100 new pharmaceutical substances are introduced into therapeutics every year. Belgium and Switzerland have each between 30 000 and 40 000 different pharmaceutical preparations on the market. The use of so many different drugs raises a host of complex technical problems with regard to quality control, nomenclature, and definition (see page 48).*

- *Although vaccination against typhoid fever has been practised for more than fifty years, controlled field trials to decide which is the most effective type of typhoid vaccine are of comparatively recent date. WHO is correlating such trials with laboratory studies in the hope of establishing standard vaccines and standard procedures for testing them (see page 61).*

TRENDS IN JUVENILE DELINQUENCY

" Juvenile delinquency does not exist in a vacuum ; it is a part of the social life of the country and it varies as the social organisation changes. Each age must find its own remedies consistent with the rest of its way of living." [1]

In 1949 the United Nations asked WHO to study juvenile delinquency, and WHO appointed a consultant whose report was published at the beginning of 1951.[2] Juvenile delinquency—this consultant (the late Dr Bovet) held—is an artificial concept, legal and social in origin. Psychologically, it involves social maladjustment; but not all socially maladjusted persons are delinquents, nor are all delinquents socially maladjusted. Proof of the artificiality of the concept is that delinquency varies with the laws in force or with the way in which they are applied. The result is that statistical comparisons between countries and between periods of time are made extremely difficult, research is hindered, and a possible source of serious error is created. Hence the need for uniform criteria and a clear and detailed picture, in the statistics, of the various kinds of offences committed.

In the study of juvenile delinquency —Dr Bovet continued—it is essential to remember that it is relatively much easier for a juvenile than for an adult to cross the comparatively low threshold separating social maladjustment from delinquency. This threshold becomes established only when psychological and moral development are complete, which may not occur till after adolescence.

The etiology of juvenile delinquency is exceedingly complex. It is clear, for example, from numerous studies that the environment is of great importance, even without the intervention of complex psychological mechanisms. Many of the children who appear before the courts are not physically or psychologically abnormal, but are merely the victims of social insecurity or the grinding poverty of their surroundings, or perhaps a combination of both. Admittedly, these social factors must set in motion a number of psychological processes if they are going to cause delinquency.

The role of somatic factors is a very controversial one. A link between mental deficiency and delinquency, which has long been accepted, is now queried. Nevertheless, it seems likely that, other things being equal, the mental defective becomes a victim of unfavourable social and psychological circumstances more readily than his intellectually normal coeval, because of his mental instability and suggestibility; and when mental deficiency and a psychopathic personality structure are found in conjunction the prognosis is very poor. The importance of organic disease and disabilities varies. Syphilis is no longer thought to count for much. Head injuries before puberty have a good prognosis. Encephalitis and epilepsy (or perhaps the epileptic temperament) may play a part in the genesis of juvenile delinquency.

What, then, of the role of psychological disturbances ? Dr Bovet pointed out that the super-ego of the child, though formed in accordance with the usual rules of personality development, may contain an antisocial element that may lead the child into delinquent behaviour. Or personality development may be partially retarded, perhaps by the emotional frustration engendered by disturbed relationships between mother and baby. The psychoneuroses do not appear to play a very important part in juvenile delinquency, but isolated neurotic symptoms do: compulsions, the need for self-punishment, the symbolic expression of repressed urges, primary or reactive aggression, the

[1] Jones, A. E. (1945) *Juvenile delinquency and the law*, Penguin Books, Harmondsworth, p. 14.

[2] Bovet, L. (1951) *Psychiatric aspects of juvenile delinquency*, (*World Health Organization ; Monograph Series*, No. 1), Geneva.

feeling of being abandoned and its various consequences. Before puberty true psychosis is rare, but psychological disorders forming a kind of " psychotic reaction pattern " may occur, with a breakdown of relations between the instincts, the ego and the super-ego; the instinctual impulses, imperfectly controlled or repressed, may then irrupt into the ego and disturb the child's adaptation to reality. In such circumstances, juvenile delinquency may readily follow.

Dr Bovet was dubious about the influence of the cinema. radio, and press, and felt that further research was needed to estimate how much they were responsible for juvenile delinquency. Research is also needed—he thought—into the suggested influence of leisure. Alcoholism has an effect on the home atmosphere, but recent genetic studies throw doubt upon the existence of the so-called alcoholic heredity, and therefore upon its suggested effect on the genesis of juvenile delinquency.

So many and so diverse have been the etiological factors propounded for juvenile delinquency that it has been labelled a bio-psycho-social phenomenon, and Dr Bovet's view was that it should be studied and combated from the three angles implied in the name. The psychiatrist, whose training is both biological and psychological, and who is interested in social problems, is well placed to co-ordinate the work of the various specialists in juvenile delinquency. There is, moreover, Dr Bovet maintained, a psychological common denominator to be found in all the aspects of juvenile delinquency, and that is the feeling of insecurity that any criminal tendency gives rise to. Insecurity gives rise in its turn to anxiety. Anxiety tends to set free aggressiveness, which may express itself in delinquent behaviour of any kind, from the mildest to the most serious. In most people this aggressiveness gives rise to feelings of guilt, which in turn produce further anxiety; and so a vicious circle is established that is one of the most constant elements of delinquency, particularly of juvenile delinquency.

Given his views on juvenile delinquency, it is not surprising that Dr Bovet held that its prevention offers a unique opportunity to rally organizations and individuals with very different points of view under a common flag for a mental health crusade; for it is clear that prevention covers the whole field of mental health. From this standpoint, he reviewed the various measures possible—outpatient treatment, institutional treatment, psychotherapy, the role of education, of social studies and social welfare, etc. Treatment should be adapted to each individual juvenile delinquent, in Dr Bovet's opinion, and be based on the fundamental laws of psychology, particularly in its emotional and subconscious aspects. The essential aim, whatever the treatment, is to enable a juvenile delinquent to build up stable and secure human relationships, as a foundation for the feeling of inner security that lies at the base of moral independence and consideration for others, without which no human behaviour can be truly adapted to the demands of society.

Ten years after Dr Bovet had visited European and American countries to gather material for his study of juvenile delinquency, another study was carried out, at the request of the United Nations, of present trends in juvenile delinquency. This study, which was intended to complement Dr Bovet's, has just been published.[3]

The author, Dr Gibbens, distinguishes in his introduction between delinquent acts that are a consequence of new opportunities for crime but do not differ essentially from more traditional forms and delinquent acts that appear to reveal a more fundamental change in behaviour or the participation of sections of the community hitherto not involved in crime.

Like Dr Bovet, Dr Gibbens stresses the importance of a correct interpretation of the statistics that purport to show a great increase of juvenile delinquency throughout the world. A rise in the incidence may be due to changes in methods of detecting offences, or to the police arresting and charging people for offences they previously ignored, or to changes in the law creating offences where

[3] Gibbens, T. C. N. (1961) *Trends in juvenile delinquency (Publ. Hlth Papr*, No. 5), World Health Organization, Geneva.

offences did not formerly exist, or to changes in the action of the courts, or to changes in the collection or interpretation of statistics. Clearly, for example, the incidence of delinquency will differ if it is defined as beginning variously at the age of 8, 13, 14 or 15 years, as in fact it is in different countries.

It has been known for a long time that convicted delinquents come mainly from the lower classes of the community and are largely concentrated in certain areas of cities, where they form a "subculture" of their own apart from the wider community. Improve the social conditions, it was argued, give these young people a chance to mix with the wider community, and the problem of delinquency will go far towards solving itself. Against this view psychiatrists pointed out that personality maladjustments are perceptible in most delinquents, and these must be dealt with before improvement can be expected. Dr Gibbens holds that the main trend in the past ten years is for these two opposing views to converge, the psychiatrist recognizing the existence of the "sociological" delinquent, the sociologist that of certain mentally disturbed delinquents. An indication of the convergence is the attention paid to groups of all sizes, from the family to the nation, and the introduction of group psychotherapy and group counselling.

Granted the existence of the delinquent subculture, how does it originate, what purpose does it serve, what preserves it and transmits it to new members? One view cited by Dr Gibbens is that the delinquent feels that he has an inferior status in the wider community; the delinquent group restores his standing while denying the values of the wider community. Clearly this view requires the formation of gangs or groups. It is supported by evidence from Norway, where most offences up to the age of 15 or 16 are committed by groups of 3 or 4 companions. The feeling of inferiority at the root of the gang's deviation from normal standards of behaviour may be linked with the way in which individual members were brought up in their families; there is often a history of neglect in overcrowded conditions where the mother has not the time to look after the individual children and give them the affection they need, or of parental maladjustment, or of rejection of the children by their parents.

The most important trend in the assessment and treatment of the individual delinquent is towards a more detailed differentiation of types of response or syndromes of delinquency. Juvenile delinquency may well be a bio-psycho-social phenomenon, but the treatment of the individual is not helped by recognition of the vast diversity of factors that may have led to his present state. Is it possible to divide delinquents into categories and approach the treatment of each category in a rational manner? Several attempts at doing so are mentioned by Dr Gibbens, each with its own merits. One of them divides delinquents into situational—the personality is essentially normal and they hardly need training-school treatment; pseudo-social—whose development has taken place within a delinquent group; personality—here there is a deeper disturbance of the personality or the pattern of delinquency is in some way rooted in it; and the asocial—the smallest and most seriously disturbed group, difficult to treat, but most likely to develop without treatment into adult asocial or amoral psychopaths. Another classification is of types of stealing (which account for the vast majority of delinquent acts) into marauding offences—stealing when opportunity presents but without planning; proving offences—usually committed alone to prove one's manhood or for reassurance; comforting offences—stealing from parents or impulsively and alone as a substitute for love or from resentment; and secondary offences—committed alone or with others, with a clear idea of what can be stolen and precautions against detection. Many of these classifications can be and are combined with each other and with classifications of the family background, a typical one of which is into the three patterns of parental rejection, parental negligence and exposure to delinquent companions, and repressive family situation.

Dr Gibbens stresses two aspects of this trend towards differentiation of various kinds of juvenile delinquents. One is that there is no clear evidence at present to show whether

the " social " or the " individual " delinquent is the more likely to become a recidivist. The other is the conclusion drawn by some workers that psychiatrists and social psychologists should pay special attention to the vital period of transition, when a youth with a clear psychological disturbance finds a solution to his emotional difficulties in a delinquent group, frequently with improvement of his mental health although at the cost of social maladjustment to the community at large.

One final biological feature that has aroused a good deal of interest in its relation to juvenile delinquency is its appearance at the age of puberty. The tendency is to regard the young as psychologically immature to a later age than formerly, and this widening gap between physical and psychological immaturity may possibly be a factor in juvenile delinquency today.

Dr Gibbens then turns to the discussion of present trends in delinquency. He asks two preliminary questions: first, what is the reason for the present anxiety about juvenile delinquency; and second, is juvenile delinquency necessary? He wonders, in relation to the first, whether the anxiety felt about juvenile delinquency at present might not be due to the greater pressure exerted by the younger on the older generation in the modern world, and the fear of the older generation lest its position of authority be threatened. As regards the second question, he says:

" There is a widespread view that a ' good ' and ' healthy ' society should not have any delinquency. No doubt this is the ideal; but so long as parents are as unstable, and the young as experimental, as they are, it is questionable whether the elimination of delinquency, even if it were possible, is really desirable. There is much to indicate that delinquency is a disorder with a comparatively good prognosis and may represent a valuable safety valve . . . From the wider aspect of mental health, it is arguable whether the elimination of delinquency in the present state of society would not generate more intractable disorders . . . Where the mental hospital population is large, the prison population is small and *vice versa*." [4]

[4] Gibbens, T. C. N. (1961) *Trends in juvenile delinquency* (*Publ. Hlth Papr*, No. 5), World Health Organization, Geneva, p. 21.

The complexity of the factors entering into the genesis of juvenile delinquency is illustrated by the disconcerting way an increase in offences in one country for what appear to be reasonable causes is not paralleled by a similar increase in another country where the same causes are operative. The international scene shows indeed almost every possible trend in property offences (the commonest) by juveniles. Certain characteristics of delinquency have always been recognized (although sometimes the evidence for them is not as solid as it might be). Thus, delinquency tends to be greater in urban than in rural societies, traditional controls being easily loosened by migration or urbanization. Urban society is more complex in its economic organization, more mechanized and standardized, more " secularized ", and more impersonal in its relations, and if the immigrant from rural areas fails to adjust himself to the entirely different life of the city he may drift into a depressed " delinquent area " in it where he is more liable to a social breakdown, or his children are brought up in surroundings conducive to delinquency, among people who are maladjusted because of physical or mental ill health, mental deficiency, alcoholism or unemployment.

Nowadays, too, in the more developed countries adolescents earn more than ever before, and the teenage market is so important that it directs advertising and marketing policy into new channels. The pressure to sell to teenagers is so great that it must have considerable social effects, the most important of which is probably to persuade teenagers that they form a separate culture, that neither of adults nor of children. Inside this group failure to earn as much as others may cause frustration and sow the seeds of delinquency.

No more than Dr Bovet can Dr Gibbens attribute juvenile delinquency to television, radio, press, or cinema, although they have all, severally or individually, been held responsible for the increase in crime and violence. Dr Gibbens sees no reason to disagree with Dr Bovet's opinion that they may determine the content of, but do not motivate, the offences of juvenile delinquents.

Another factor that may have some influence, even if only indirectly, on delinquency is the trend towards equality between the sexes. It may provide an economic basis for the greater frequency of divorce and separation, with their consequences on family life. Increased independence of women may also lead to a " devaluation " of inadequate fathers hitherto supported by a cultural pattern of male superiority, and to an abdication of their responsibilities as fathers. Indeed, the role of the father in the family has recently been given much more attention than formerly, partly, no doubt, by way of reaction against the dominant role previously assigned to the mother. When the father abdicates his responsibilities, leaving it to the mother to bring up the child, the boy after puberty may over-value rebellious behaviour, indulging in " proving " offences like stealing cars to reassure himself about his courage, independence, and virility. Not so girls, who tend to nurse their grievances and anxieties until adolescence, when they may indulge in wayward or sexually promiscuous behaviour, or until adulthood, when they appear as the rejecting or unstable mothers of the next generation's delinquents. In many families both parents often suffer from tensions, psychological disabilities and minor nervous breakdowns. They try to bring up their children properly but cannot conceal their conflict, and so rear insecure children who may unwittingly be encouraged in the sort of behaviour that their parents have tried to prevent.

Has there been any marked change in the types of offences committed by delinquents? Stealing has increased in some countries, but whether the stealing of cars and gramophone records is a new crime or merely a new opportunity is a matter of doubt. Sex crimes do not appear to have increased greatly among adolescents, and the increase in violent crime appears to be moderate; nor is there any general concern about an increase in alcoholism and drug addiction. On the other hand, there does appear to be a distinct increase in hooliganism—loud, aggressive or insulting behaviour in public, wanton damage to windows, street lamps, cars, obstruction of cars, etc.—indulged in by groups of youths who have received a distinctive name in nearly all European countries and often wear distinctive clothing differentiating them from members of the public in general.[5] This has always occurred to a certain extent, and differs from the curious riots that have taken place in some countries, where the numbers involved are more than 50 and sometimes several hundred, but there is no organized leadership, the riots are not promoted or secretly planned, and the youths responsible usually have no delinquent record, do not come from broken homes, have a good work record, and often do not know why they have taken part. The reasons for these displays may lie in hostility to the older generation, the insecure state of the world today, the legacy of the disturbances of the war, a growing cynicism and loss of the values linked with religion, or perhaps the absence in modern society of those ritualized opportunities for free emotional expression, furnished by the ritual festivals of primitive people or the carnivals, fêtes and celebrations of older generations. They can, indeed, hardly be regarded as examples of juvenile delinquency, which appears to arise, as it always has, from deprivation and major disorders of family life.

The multiplicity of factors entering into the causation of juvenile delinquency necessitates a broad approach to its prevention. All measures for the promotion of the health and well-being of children are helpful. But the problem of preventing juvenile delinquency is complicated by the fact that successful prevention often involves measures that tend to delay emotional maturation, and this leads to crime at a later age.

In the field of general psychiatry, two main general trends in prevention have been perceptible: first, an extensive development of the public health aspects of psychiatry as applied to whole communities or sub-communities; second, a more concentrated study of the physiological and biological basis of the individual patient's disorder, which can be regarded as a breakdown in the balance

[5] These youths are called hoods (short for hoodlums) in the USA, *blousons noirs* in France, *Halbstarke* in Germany, *nozems* in the Netherlands, *laerjakker* in Norway, *chuligani* in Poland and Czechoslovakia, *skinn knutter* in Sweden, teddy boys in the United Kingdom, and *stilyagi* in the USSR.

between the stresses imposed and the individual's capacity to resist them. This balance depends on the personality and intelligence of the individual, his desire or incentive to achieve it, the size of the task involved, and the general setting in which he has to achieve it. Help can be given him in dealing with any or all of these factors.

In research into ways of preventing juvenile delinquency two trends are of special importance. One is the development of prediction studies—studies on how to identify young children who are in danger of becoming seriously delinquent; the other, the designing of preventive programmes that can be scientifically evaluated. Prediction studies depend on the finding that prediction weights can be given to each of certain characteristics of the family background, the total social prediction score indicating the likelihood of the child's becoming a future delinquent. If the risk is great, preventive work can be concentrated on the child so indicated.

Experiments in new methods of prevention have been tried in various parts of the world. In the Chicago Area Project it is recognized that social cohesion and the community spirit cannot come from outside but must come from the natural leaders of the community, who are encouraged to build up their own organization (assisted tactfully from outside). In London, family-relation clinics use group discussion. Attempts have been made to work with pre-delinquents in their natural groups, providing them with opportunities for success and achievement by schemes that will awake their enthusiasm and hope.

Apart from these experiments in prevention, the mental health aspects of medical care, the emotional needs of children, the realization that delinquency is a failure of education (whether parental or national) have all led to a greater emphasis among doctors, teachers, and the police upon a positive approach to the prevention of delinquency. As well as special schools for the mentally and physically handicapped, the abnormal and the educationally maladjusted, special " all-day schools " have been tried out in the City of New York and in Israel, with additional staff and more varied curriculum.

Probation treatment is widely used for the minor delinquent. Although there is a growing tendency to treat mental patients outside the hospital, there is no such tendency as yet to treat the disordered delinquent outside an institution. Institutional treatment is being more and more differentiated and now there are three types: a more or less standard type for the majority of rather serious offenders; a more specialized long-term type for severely disordered offenders; and, more recently, a short-term type for those who can no longer be treated on probation but are not sufficiently delinquent to warrant long terms of treatment. Failure with the second type is common, and the delinquents are generally counted a psychiatric problem; group psychotherapy taking into account the whole range of their relationships with each other and the entire staff is being tried. The argument in favour of the third type is that a short absence from their usual environment will help them towards a change in outlook; but this is at best not a very strong argument, unless the short stay in an institution is merely the prelude to a period of supervision.

Finally, the importance of after-care is now being realized. No treatment of delinquency can be complete unless there is adequate after-care.

HEALTH IN THE CONGO

Dr M. G. Candau, Director-General of WHO, told the twenty-sixth session of the WHO Executive Board that if political stability and normal administration could be guaranteed in the Republic of the Congo (Leopoldville), the medical problems would not be difficult. As matters stood—he went on to say—there must be no illusions about the fact that the health situation was bound to deteriorate month by month and WHO's task was to prevent the worst from occurring.

Dr S. Btesh, WHO Adviser on Medical Care to the Ministry of Health of the Congo, discusses below some of the health problems of the country and the steps taken by WHO to deal with them.

Before the crisis

The general situation of the health services in the Congo before the crisis occurred was satisfactory. Under a plan adopted by the Government in 1945, a decentralized system of medical care had been organized, health services being based on the regional hospitals (*centres medico-chirurgicaux*) and their satellite clinics or health centres. Each of these " health units " or *secteurs médicaux* provided medical care and personal preventive services for a population of between 80 000 and 140 000. A 10-year programme for the construction of hospitals and health centres had been started in 1949, and by 1959 had almost reached its goal. Most of the regional hospitals and some of the provincial hospitals are now housed in modern, well-planned buildings with complete and up-to-date equipment.

The preventive services had not reached the same degree of decentralization. They were based on a network of central and provincial institutes of hygiene, dealing with urban sanitation and the countrywide control of endemic and epidemic diseases (immunization, vector control, chemoprophylaxis, etc.). A special feature of these services was the mobile health teams, led by European sanitarians and operating in both urban and rural areas, screening the population for the major endemic diseases. About one-third of the indigenous population was screened in this way every year. A very efficient supply system had been set up with a large central depot in Leopoldville and provincial stores. The equipment and medical supplies provided were of very high quality and more than sufficient in quantity. In fact, in many cases they gave an impression of lavishness.

All the health services were directed and supervised by European administrative and technical personnel, Congolese personnel filling the auxiliary and lower grade posts. There was therefore complete dependence on European staff, there being no Congolese personnel sufficiently trained to fill posts at administrative and supervisory levels. Plans for the training of such personnel had been worked out, however, and a start had been made with the admission of Congolese students to universities, both in the Congo and in Belgium. However, by 1960 there was not a single Congolese doctor or graduate nurse. The first two Congolese doctors were expected to graduate in 1961, and the first four Congolese nurses in 1962.

The crisis

Disintegration of the health services began to be noticed towards the end of 1959. The first symptom was antagonism on the part of the population towards the activities of the European sanitarians: people began to refuse vaccination and failed to attend for medical screening by the mobile teams. By July 1960 vaccination and screening had ceased completely in the rural areas and in many of the urban areas. About this time an exodus of European personnel began; two-thirds of the doctors, all the civilian graduate nurses, and

the great majority of the European sanitarians left the country. About 150 Congolese medical assistants and 1000 male nurses were left to carry on the medical work. Most of the regional hospitals were depleted of European personnel and only the provincial hospitals continued to function, though with restricted staff. Preventive services were discontinued altogether; organized vaccination programmes and vector control measures ceased, while the water supply installations were left in the hands of untrained Congolese workers. The medical supply system was disorganized, for, though the central depot and many of the provincial stores had adequate supplies, these could not reach the more distant areas for lack of transport facilities. In general, there was no loss of supplies or equipment through theft or wanton destruction. However, some loss occurred through lack of proper maintenance or misuse due to ignorance.

International action

Following an appeal by the Security Council, the Secretary-General of the United Nations asked WHO to help deal with the emergency and to convey a similar request to the International Committee of the Red Cross and the League of Red Cross Societies. A team of WHO advisers proceeded immediately to the Congo and placed its services at the disposal of the Government. A survey of the situation revealed that the principal emergency was in the field of preventive services and environmental sanitation. The medical care services had suffered less, since the Congolese auxiliaries continued to carry out routine examinations and treatment of patients in the clinics and health centres, and cases of major surgery were referred to the provincial hospitals. On the preventive side, however, services were completely paralysed. Shortly after the arrival of the WHO team, national Red Cross Societies (at the request of the International Red Cross bodies) and some governments started sending emergency medical teams composed of doctors and nurses. By the middle of August there were 34 teams from 20 different countries; 27 of these teams were sent by national Red Cross Societies and 7 by national governments.

The function of the WHO advisory team was twofold. It had to assist the Government in meeting the immediate emergency and it had to advise it on the long-range planning of an efficient health organization. It fulfilled the first function by acting as a co-ordinator of the medical emergency teams, both Red Cross and national. These teams were distributed among the various regional centres and put in charge of hospitals, clinics, etc. A number of public health personnel had to be recruited immediately to deal with such pressing problems as safe water supplies, vaccination campaigns and vector control. The long-term action of WHO consisted in drawing up detailed plans for the organization of health services, the recruitment of personnel and the training of Congolese medical and paramedical personnel. The principal aims of the WHO plan are as follows:

(1) to adapt the existing structure and organization of the health services to the changing needs of the country;

(2) to recruit international personnel for the efficient operation of the medical care and preventive services;

(3) to embark immediately on an extensive programme for the training of local personnel.

It is estimated that the minimum number of foreign personnel that will have to be recruited from abroad for the next 10 to 15 years is between 700 and 800, including doctors, engineers, sanitarians and other technicians. Programmes have already been started to accelerate the training of Congolese personnel to take over key positions as soon as possible. Thus, 60 Congolese medical assistants have been admitted to 5 schools of medicine in France, starting in the fourth year of the regular course which leads, 3 years later, to the degree of Doctor of Medicine. Assistance was given to the Lovanium University to increase its annual intake of students of medicine from the present number of between 10 and 15 to as many as 40. Fellowships were

offered to undergraduates, and 7 of them have started their medical studies in France and in Switzerland (Geneva). On-the-job training programmes for nurses, administrators, laboratory technicians, etc. will soon be initiated, enabling Congolese personnel to fill key positions in hospitals, laboratories, etc. These are just a few examples of how WHO is hastening the training of Congolese staff.

Danger of outbreaks of disease

There is no doubt that the country is threatened to varying degrees with outbreaks of such endemo-epidemic diseases as smallpox, plague, malaria, sleeping sickness, yellow fever, tuberculosis and yaws, all of which had been kept under control for a number of years. It is estimated that over 80% of the population had been immunized by primary vaccination and revaccination; there were still, however, between 3000 and 4000 cases of smallpox a year, the majority being of the modified type (alastrim). There is a very real danger that the migrations now taking place as a result of tribal conflicts may cause the disease to spread.

Malaria control measures in the Congo were confined to insecticide spraying and chemoprophylaxis and there was no malaria eradication programme. There were still about 1 million new cases of malaria every year and no decline in prevalence during the last 5 years, though malaria control seems to have been quite efficient in the urban areas. There is now a real danger that the disease may spread to those areas unless active preventive measures are resumed.

The following steps were taken to avoid possible epidemics.

1. A simple scheme for obtaining information about the prevalence of certain diseases was worked out. WHO provided advisory personnel at the provincial level and a number of mobile teams which were assigned to the rural areas. These WHO workers are in continuous contact with the hospital dispensaries and report weekly to the Chief WHO Adviser in Leopoldville on all cases of communicable diseases admitted to hospital or diagnosed in the various areas. The WHO adviser is in a position to dispatch specialized personnel to areas where an increase in the prevalence of a disease is reported.

2. The WHO mobile teams have re-established routine vaccination and chemoprophylaxis in the areas to which they have been assigned.

3. A WHO malaria control team composed of a malariologist and an entomologist pays regular visits to various regions, and reports on the situation to the Chief WHO Adviser in Leopoldville, who brings the information to the notice of the Ministry of Health and the WHO provincial advisers.

4. Five WHO sanitary engineers have been placed in the provincial departments of health to advise on problems of environmental sanitation, including water supplies, vector control and food hygiene, while technicians have been assigned to the water supply plants of the most important cities to ensure proper supervision of the filtration and chlorination of water.

Other health problems

The Congo enjoys a plentiful supply of food (vegetables, fruit, oil, fish and game). Prior to the present disturbances, this food was easily obtainable by the population, so that malnutrition in the Congo was not due to lack of food but rather to faulty habits. The most important type of malnutrition was protein deficiency; kwashiorkor is extremely common and so are various types of iron deficiency anaemias. During the disturbances, the situation was changed mainly because of unemployment, dislocated communications, and fairly extensive tribal migration. These three factors created serious nutrition problems in certain urban and suburban communities that were particularly affected by the economic crisis. More serious, however, were the problems of the refugee tribes in some of the more disturbed areas, who were cut off from their usual sources of supply.

The prospect for the future

The future prospects of the health services in the Congo are good, provided sufficient personnel can be recruited to fill the present

gap. The Congo will require international assistance in two fields, namely: intensive education and training of local personnel; and provision of foreign personnel for many years to come pending the training of a sufficient number of local personnel.

There is no doubt that the high standard of the health services enjoyed by the population in 1959 cannot be immediately re-established. However, the WHO programme aims at restoring a satisfactory standard over a period of several years.

QUALITY SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS *

The number of pharmaceutical preparations is increasing very rapidly. Those used by the previous generation were, in general, different from those used today, and in comparison very few; and it may safely be predicted that those prescribed by the next generation of physicians will nearly all be different from those prescribed at present. Over 100 new pharmaceutical substances are introduced into therapeutics every year. Their average life at present is between two and five years, and seems to be diminishing all the time, owing to the large amount of money and energy spent on research and the tremendous competition between pharmaceutical firms and institutes. Yet nearly all the new substances used in pharmaceutical specialities throughout the world are created in a limited number of countries. By co-ordinating the information provided by these countries on the quality examination and introduction of the new substances, it is to a certain extent possible for WHO to propose principles and specifications for the quality control of pharmaceutical preparations produced and imported by Member States.

The number of pharmaceutical specialities and preparations available to the physician and the public varies greatly from country to country, according to resources, limitations of various kinds imposed by governments, currency difficulties, etc. For instance, Belgium and Switzerland have each more than 30 000 different pharmaceutical specialities on the market. On the other hand, Denmark has kept the number of pharmaceutical specialities down to 2000, and in certain countries where the production and distribution of pharmaceuticals is nationalized, comparatively small numbers of pharmaceutical substances are placed at the disposal of the physician.

The terms "pharmaceutical preparations" and "quality control" are used here in preference to "drugs" and "control" to avoid confusion with the control of addiction-producing drugs exercised by the United Nations. The following definitions appear in the report of a WHO Study Group on the Use of Specifications for Pharmaceutical Preparations:[1]

"(1) a drug (or pharmaceutical preparation) is any substance or mixture of substances manufactured, sold, offered for sale or represented for use in:

(*a*) the diagnosis, treatment, mitigation or prevention of disease, abnormal physical state or the symptoms thereof in man or animal;

(*b*) restoring, correcting or modifying organic functions in man or animal.

"(2) A pharmaceutical speciality is a simple or compound drug ready for use and placed on the market under a special name or in a characteristic form."

The Study Group "expressed the view that the above definition of a pharmaceutical preparation is better than one which defines a drug as a substance named in an official list. Although the latter definition may be

* Based on an address given by Mr P. Blanc, Chief, Pharmaceuticals, WHO, at the Fifth Pan-American Congress of Pharmacy and Biochemistry, Santiago, Chile, 12-19 November 1960.

[1] *Wld Hlth Org. techn. Rep. Ser.*, 1957, 138, 14-15.

easy to apply, it is weak in at least one important aspect—namely, that a manufacturer can avoid having to submit a preparation to government control by making it slightly different in its chemical composition from other preparations of the same class which may be included in the list, or, in the case of a vegetable drug, by using a drug from a closely related plant ".

It is the aim of the national authorities dealing with the examination of pharmaceutical preparations to have adequate quality specifications for preparations sold in their respective countries. Appropriate specifications for most of the substances and pharmaceutical forms used to be included in the national pharmacopoeia and medicinal substances coming on the market were added to the list to keep it more or less complete. However, many countries cannot undertake the enormous amount of work needed to establish official specifications and they therefore adopt those of other countries or, in a number of cases, those proposed by WHO in the *International Pharmacopoeia*. In many countries the quality control of pharmaceutical preparations imported or locally produced is still inadequate.

Mention has been made of the *International Pharmacopoeia*, the title of which dates from a period when it still seemed possible to assemble, under an international authority, a collection of specifications that could be adopted by the various countries of the world. Today this is possible only in part, and WHO accordingly concentrates on the more important pharmaceutical substances used in different countries. The *International Pharmacopoeia* constitutes "a collection of recommended specifications, which are not intended to have legal status as such in any country, but are offered to serve as references so that national specifications can be established on a similar basis in any country ".[2] There are many indications that these recommended specifications are used by countries as an important basis for the establishment of their national specifications.

WHO has issued a two-volume first edition of the *International Pharmacopoeia* and a *Supplement*, covering in all 500 medicinal substances and pharmaceutical forms—injections, tablets and a limited number of tinctures. These three volumes were originally published by WHO in English and French, and subsequently in Spanish; several thousand copies have been sold of these editions. In addition, with the authorization of the Director-General of WHO, translations have been published by the authorities of certain countries. There are now German, Japanese, and Korean editions.

In general, the specifications include the name and the chemical formula or other definition of the substance, then a description, indications concerning solubility, and identification tests. In certain cases identification has become difficult. When an important new pharmaceutical substance is introduced into therapeutics, it is often followed by many other substances with formulae very close to that of the original product.

The specifications usually include a physical, a chemical and, less frequently, a biological assay. Other tests may relate to pyrogens, or the maximum permissible amount of impurities. There are also specifications on storage, and there are suggested daily and maximum doses for children and adults. The co-operation of pharmacologists, clinicians, paediatricians and other experts was required for the difficult task of establishing these doses, which have been submitted to the World Medical Association. While the recommended tests employ a number of the so-called classical methods such as titrimetry, newer methods are being introduced—for example, complexometry and titration in non-aqueous media, particularly glacial acetic acid, and chromatography.

The specifications include methods for determining freezing and boiling ranges or points, for the determination of chloride, sulfate and lead, for microbial assays of antibiotics, for the determination of nitrogen, the determination of optical rotation, etc. Sterility tests for injectable preparations are given, and sterilization methods: heating in an autoclave; heating with a bactericide; and

[2] *Off. Rec. Wld Hlth Org.*, 1950, 28, 9 (Resolution WHA 3.10).

filtration. Sterilization by irradiation is not yet officially recognized.

Spectrophotometry, the science of measuring the absorption by substances of electromagnetic radiations of definite and narrow wave length, will probably be dealt with on a larger scale in the second edition. The range extends from the shorter wave lengths of the ultra-violet, through the infra-red. Ultra-violet spectrophotometry was already described in Volume I of the *International Pharmacopoeia* for the determination of Vitamin A, while infra-red spectrophotometry is increasingly used by national control laboratories for the identification of pharmaceutical substances, notwithstanding the fairly high cost of the instruments required. The recent new edition of the *Pharmacopoeia of the United States of America*, for instance, includes the use of infra-red spectrophotometry for identification tests in a number of monographs, and the WHO Expert Committee on Specifications for Pharmaceutical Preparations considered that, in its second edition, the *International Pharmacopoeia* could make use of infra-red spectrophotometry for some substances.

In preparing specifications, WHO is, of course, greatly dependent on the work of the national pharmacopoeia commissions, specialized laboratories and other interested institutions in countries where they are sufficiently well informed and active to be able to keep pace with the increasingly rapid production of new medicinal substances. The pharmacopoeia commissions in the United States and Great Britain are doing remarkable work in this field. WHO co-operates closely with these and other commissions including the commission of the *Nordic Pharmacopeia*, which is to be published as the first inter-country pharmacopoeia.

WHO endeavours, through specialists and their laboratories in different countries to stimulate and co-ordinate laboratory work on specifications. In principle, specifications are issued as mimeographed documents, then submitted to governments and eventually published in the *International Pharmacopoeia*. Whether this system works altogether satisfactorily with the limited staff and means available is open to discussion; however, the Organization can depend on the efficient co-operation of a number of specialists and their laboratories in different countries and it is hoped that the work can be developed at a sufficient rate to be of direct help to all Member States.

The difficulties involved in the laboratory control of a new pharmaceutical preparation are great and, however skilful the analyst, it cannot always be certain that changes will not intervene after manufacture to make a preparation unsafe, as for example in the case of capsules recently put on sale in one country with tragic results, although laboratory analysis, pharmacological and clinical tests appeared to have demonstrated their quality and safety.

When should authorities agree to the introduction on the market of a new pharmaceutical substance ? This is a complex question and regulations differ widely from country to country. There may be special requirements for new preparations not yet recognized as safe. In the United States, such drugs are referred to as " new drugs ", and cannot be sold until their safety in the normal doses has been officially approved. Similar procedures are being adopted in some other countries.

Even with all the necessary information it is difficult for officials to take a decision. How far are the pharmacological and clinical data on new preparations supplied to the appropriate authorities in the country of manufacture acceptable in other countries ? What universal criteria could be developed for pharmaceutical quality control ? There should be increasing co-ordination between the authorities who deal with the introduction of new pharmaceutical preparations in different countries. In this respect WHO is a useful co-ordinating agency for the international exchange of specifications for laboratory control and also of the results of pharmacological and clinical trials, in particular for drugs used in mass campaigns against specific diseases, such as bilharziasis, leprosy, etc.

Permission to introduce a new drug is generally based on the evidence of its safety,

claims concerning its therapeutic action being usually the responsibility of the manufacturer. The information to be included on the labels of new pharmaceutical preparations differs from country to country, and in this respect WHO is already helping to bring about a welcome standardization, e.g., in the naming of the substance, the units of measurement, the expiry dates, etc.

It has also been suggested that, when considerations of safety demand it, a new drug could be kept off the market until the manufacturer's representations regarding the reliability of manufacturing methods, facilities, and controls have been confirmed by an inspection, to verify whether the firm can ensure the identity, strength, quality and purity of the preparation. National authorities cannot be expected to undertake analysis of all batches—or even a certain number of batches—of a preparation to ensure that its quality is consistent; this applies with special force in some countries where there may be shortages of trained laboratory staff. It should be mentioned that WHO is helping to remedy such situations by providing fellowships on the quality control of pharmaceutical preparations.

The present introduction of so many new pharmaceutical preparations creates difficulties for the authorities dealing with their quality control. They must determine the quality of each product, as well as judge whether the information submitted by the manufacturer is adequate to ensure its safety in the conditions of use recommended, and whether the claims made for it are supported by pharmacological and clinical tests. The critical scrutiny of this information must be done by experts, each familiar with one aspect of the control process and actively engaged in his own field of medical or experimental science. The laboratory work on quality control is difficult, requiring much care and patience and bringing little recognition. Good specialists are hard to find.

There is also the problem of classifying pharmaceutical preparations into those which can be dispensed on prescription or sold directly to the public. It is difficult to know at the outset into which category a new preparation should be placed, and it can be months or years until misuse, secondary effects or other factors indicate that it should be sold only on prescription.

Finally, mention should be made of the work being done by WHO on a related problem, that of preventing confusion due to the use of different non-proprietary names for the same pharmaceutical preparations. The authorities and manufacturers in different countries are co-operating by sending WHO requests concerning new pharmaceutical substances to be introduced on the market. With the help of a number of experts, names are then selected to be proposed as international non-proprietary names. In this way names for more than 800 medicinal substances have been proposed and published in the *WHO Chronicle* and other journals.

Epidemiological studies of tuberculosis

"The epidemiology of tuberculosis varies considerably in different countries. It is important for countries to make local epidemiological studies to determine as precisely as possible in which population groups the tuberculosis problem is concentrated and how the disease is being spread in the areas concerned. For example, in some areas household exposure seems to be very important in the spread of the disease while in others it does not seem to be of greater significance than other types of exposure."

From the seventh report of the WHO Expert Committee on Tuberculosis (*Wld Hlth Org. techn. Rep. Ser.*, 1960, 195)

INTERNATIONAL WORK IN CHOLERA *

2. The cholera vibrio

As early as 1819, the Bengal Medical Board reached the conclusion that cholera is due to a " pestilential virus " acting primarily on the stomach and small intestines; it was, however, unable to accept the idea that cholera is contagious. This hypothesis first began to gain adherents in 1831, and in 1849 received strong support from John Snow and William Budd. During the second half of the nineteenth century, various workers claimed to have seen the germ responsible for cholera in the stools or vomits of patients, but they did not succeed in isolating and cultivating the organism.

When the fifth pandemic reached Egypt in 1883, two commissions—one French and one German—were sent there to search for the cholera microbe. While the French team attempted first to reproduce the disease in animals, the German team under Koch concentrated on culturing and isolating the organisms from the infected tissues of cholera victims. In this they succeeded, and Koch named the organisms " comma bacilli " on account of their curved appearance (see figure). Continuing his research in India, he was able to show that these bacilli were invariably present in the dejecta of cholera patients but disappeared as the patients recovered. The conditions under which these findings were made must have been particularly favourable because later workers were often unable to demonstrate the presence of the comma bacilli in patients apparently suffering from typical cholera or in the intestines of victims of the disease. On the other hand, comma-like bacilli—or vibrios as they were subsequently called—were soon found to be of common occurrence, without necessarily having a pathogenic action. Intensive laboratory studies were therefore initiated to determine the characteristics of the *Vibrio cholerae* that would distinguish it with certainty from the cholera-like vibrios.

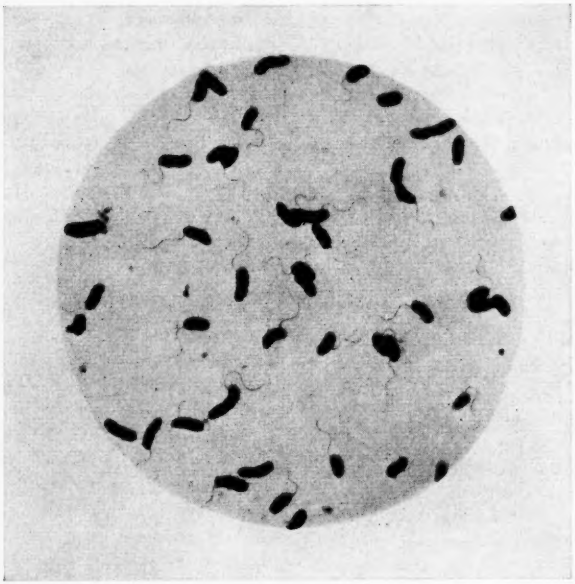
General appearance

The name " vibrio " was given to the cholera bacillus because of the rapid " scintillating " or " darting " movements that are imparted to it by the long flagellum—4 or 5 times the length of the body—clearly visible in specially stained cultures (see figure). The body itself measures 1.5-2 microns in length by 0.3-0.4 microns in breadth. Considerable variations in length may be observed under the microscope, however, depending upon the degree of curvature and whether the plane of curvature is parallel to that of the visual field. Some of the vibrios may be twisted into the shape of a letter " S ", or two or more vibrios may adhere together, particularly in older cultures, to give larger " S " forms or even long spirals. Cultures should therefore be fresh and grown under carefully standardized conditions. Among other factors, it is important that the medium should be sufficiently alkaline. A pH of 8-9 is well tolerated by cholera and other vibrios, but inhibits the growth of most contaminating bacteria. The pH tends to fall during cultivation and measures have to be taken to counteract this.

As first noticed by Berestneff in 1908, if cholera vibrios are repeatedly subcultured on agar the appearance of the colonies sometimes undergoes a marked change. When examined microscopically under low power, the colonies appear larger and thinner, with irregular, jagged outlines. This is known as the rough or R form of the cholera vibrio, in contrast to the smooth or S form of the initial cultures. The phenomenon of dissociation, i.e., the transition from smooth to rough, has been exhaustively studied. The main difference

* This is the second in a series of articles intended to give a concise account of the public health aspects of cholera and to outline present trends in its control. The first of these articles appeared in the January number of *WHO Chronicle* (1961, 15, 3).

18-HOUR CULTURE OF *VIBRIO CHOLERAE* ON NUTRIENT AGAR



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between the two forms appears to be that the cells of the S form, after undergoing division, slide past one another easily, forming a smooth compact mass, whereas the cells of the R form tend to adhere together to produce branching chains and irregular masses, so that the final cluster has a jagged, uneven appearance. When cultured in broth or peptone water, the S strains produce marked and uniform turbidity and sometimes form a thin pellicle on the surface of the medium, whereas the R strains form a thick pellicle and granules that sink or remain partially suspended, causing only a slight turbidity. Studies by Bruce White have established that whereas the S form secretes 4 specific polysaccharides the R form secretes only 3. He also discovered a ρ variant which secretes only 2 of these polysaccharides. The picture is further complicated by the existence of a so-called rugose form, which presents a corrugated appearance on agar and, unlike either the S or the R form, is adherent to the medium. Bruce White showed that rugosity is the result of an abnormally active secretion of a mucinous material. The rugose variants readily revert to the S, R or ρ forms from which they are derived, but they appear to be more resistant to unfavourable growth conditions, so that the mucinous material may be a protective secretion.

Haemodigestive and haemolytic properties

There has been much controversy regarding the behaviour of cultures of *V. cholerae* and the cholera-like vibrios in blood-containing media. As early as 1884, Koch noticed that, when cultures were prepared from blood-containing stools, clear zones appeared around the cholera colonies. He believed this to be due to a haemolytic action, a view also shared by several later workers. It is now known, however, that the clear zone, or halo,

which appears around the *V. cholerae* colonies grown on blood-agar plates is not the result of haemolysis, but is due to the action of proteolytic enzymes secreted by the vibrios. If fluid cultures of true cholera strains, or filtrates of such cultures, are added to suspensions of red blood cells, no haemolysis takes place. On the other hand, if cultures of cholera-like vibrios are used, lysis of the red blood cells often occurs with release of haemoglobin. Since, however, some of the cholera-like vibrios do not produce this phenomenon, the differential diagnostic value of such tests is limited. Moreover, for reliable results, careful attention must be paid to the technique used, and especially to the choice of a suitable type of blood. Human blood is unsatisfactory, but goat, sheep and calf blood have all been recommended.

The so-called El Tor vibrios have been a source of considerable confusion. These were first isolated by Gotschlich in 1905 from dead bodies of pilgrims who had returned from Mecca at the quarantine camp at El Tor. Although the victims had shown no sign of choleraic disease, all the tests applied by Gotschlich to the organisms isolated appeared to indicate that they were true cholera vibrios. It was later discovered, however, that, unlike *V. cholerae*, they caused haemolysis of red blood cells. At the same time, they produced an exotoxin which was rapidly lethal to experimental animals. Later workers have isolated similar haemolytic vibrios during outbreaks of true choleraic disease. The demonstration of haemolytic activity is not therefore sufficient, by itself, to exclude pathogenicity, but other tests, described below, permit a differentiation of these El Tor strains from other haemolytic cholera-like vibrios.

Although both *V. cholerae* and El Tor vibrios, when grown on blood-agar plates, produce colonies surrounded by haloes, the appearances are not identical. If a comparison is made after 48 hours, the whole of the *V. cholerae* plate is seen to have changed in colour from red to brown as a result of the conversion of haemoglobin to methaemoglobin, whereas in the case of El Tor vibrios, clear zones are seen immediately surrounding the colonies, where haemolysis has occurred, but the colour of the remainder of the plate is unchanged. It could be shown spectroscopically that the zones surrounding El Tor colonies contain haemoglobin, released by haemolysis, whereas no haemoglobin is present in the *V. cholerae* zones, the pigment having been broken down by the action of the proteolytic enzymes (haemodigestion). This difference in properties forms the basis of one of the tests recommended for the laboratory diagnosis of cholera.[1]

Antigenic structure

The agglutination test for the identification of cholera vibrios was introduced by Gruber & Durham in 1896. Immune sera were prepared by injecting killed cultures of authentic *V. cholerae* intraperitoneally into guinea-pigs. Dilutions of these sera in broth were then mixed with broth suspensions of the organisms to be tested. Both macroscopic and microscopic examinations were carried out, and if agglutination was confirmed it was concluded that the suspect strains were true cholera vibrios. Further studies, particularly by Balteanu (1926), demonstrated that *V. cholerae* contains two series of antigenic substances—a thermostable or O antigen and a thermolabile or H antigen. The O antigen causes agglutination in large, loose flocculi, whereas the H antigen causes agglutination in small, compact granules. Isolated flagella behave as though composed entirely of H antigen, and the two components have therefore also been termed "somatic" and "flagellar" antigens. The somatic antigen is stable for considerable periods at 100°C, while the flagellar antigens are destroyed at this temperature. Shousha demonstrated in 1931 that the thermolabile flagellar antigens of El Tor vibrios are identical with those of *V. cholerae*, but the thermostable somatic antigens are quite different in the two strains. By performing the agglutination reaction with cultures that have been adequately heated to destroy the H antigens, it is thus possible to distinguish between the two strains.

[1] Burrows, W. & Pollitzer, R. (1958) *Bull. Wld Hlth Org.*, **18**, 275.

This can also be done by using heated cultures to prepare the immune sera, which are thus obtained free from H agglutinins.

From research carried out over the last 30 years, it is evident that the antigenic structure of cholera vibrios is highly complex and susceptible of considerable variation. Different workers have arrived at conflicting conclusions and many problems remain to be solved. It is generally accepted, however, that there are at least two distinct serological races of *V. cholerae* and El Tor vibrios, known as the Ogawa and Inaba types, and possibly a third type (Hikojima) with an antigenic composition intermediate between that of the other two. Furthermore, dissociation is accompanied by changes in antigenic structure, the rough and the ρ forms being less specific in their serological reactions than the smooth forms. It is consequently important to use the smooth forms for the agglutination reaction.

There is thus an urgent need for further research on the antigenic structure and serological reactions of cholera and cholera-like vibrios. As stated by a WHO Expert Committee on Cholera in 1952, however, " the present definition of the cholera vibrio, though incomplete, is sufficient for practical purposes " and the value of the tests adopted for laboratory diagnosis is not lessened by the necessity for further serological studies.[2] These studies are being actively encouraged by WHO, and an Expert Committee on Biological Standardization has greatly enhanced the reliability and comparability of the laboratory procedures by establishing International Reference Preparations of cholera agglutinating serum and cholera antigen, both of the Ogawa and the Inaba types.[3]

Vitality

Cholera vibrios are not very resistant to heat. They are killed within a few minutes at 80°C (dry heat), and growth can be prevented in inoculated tubes by heating for 10 minutes at 60°C or for 5 minutes at 65°C. On the other hand, the vibrios are remarkably resistant to low temperatures. Cultures in broth, gelatin and agar have been shown to tolerate temperatures below −30°C and to remain viable in a completely frozen condition for 20 days.

The length of survival of dried cholera vibrios has been reported as varying from a few hours to several days, or even months, depending, apparently, upon the rate of drying, the thickness of the layer, the nature of the medium, and possibly other factors. Freeze-drying has been found to be an excellent method of preserving both the viability and the immunogenic properties of *V. cholerae*. Sunlight kills the vibrios within a few hours, while ultra-violet light and, especially, X-rays are still more lethal.

The organisms are extremely sensitive to acids, being killed in a few seconds by concentrations of hydrochloric or sulfuric acid as low as 1/10 000. It is interesting that *V. cholerae* were found to be killed immediately by the gastric juice of a patient suffering from hyperacidity, but survived for 24 hours in the gastric juice from a patient with hypochlorhydria. It is thought, however, that if ingested with a copious draught of water or enclosed in a mass of food, the vibrios might pass unharmed even through the acid stomach.

The usual disinfectants are lethal to cholera vibrios, and so are a number of other substances having an antiseptic action, especially potassium permanganate and copper sulfate. Chloride of lime kills more rapidly than quicklime.

The length of survival of cholera vibrios in stools and in sewage is obviously of considerable interest. Discrepant findings by different workers have been shown to be due mainly to temperature differences. Whereas the organisms survived up to 8 days in a specimen of a cholera stool kept in the refrigerator, they died within 3 hours in another specimen of the same stool kept at body temperature. Longer periods of survival, up to 30 days or more, have occasionally been reported. The viability of the organisms on a variety of contaminated materials has been investigated, particularly on foodstuffs. In general, the organisms do not survive for

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1952, **52**, 6.
[3] *Wld Hlth Org. techn. Rep. Ser.*, 1954, **86**, 7.

more than 2 or 3 days, even on fruit and vegetables. On meat and fish, they may remain viable longer—possibly up to 2 weeks if stored at a low temperature. The survival time in water again varies within wide limits, depending upon the organic content of the water and the temperature. At a temperature of 6°C, for example, the vibrios were found to survive for at least 20 days in river water in Europe. On the other hand, in the raw water of the Gangês and Jumna rivers in India they died within 2 hours, but when the water was previously boiled the survival time was much increased, probably because of the destruction of competing bacteria.

Toxin production

Koch's original hypothesis was that cholera is caused by the action of a toxin excreted by the causative organisms. It was soon shown, however, that filtrates of cultures of *V. cholerae* produced signs of intoxication in dogs only if the cultures were more than several days old. This suggested that the toxin was released on the death of the organisms rather than excreted while they were alive, and numerous subsequent observations have confirmed that an endotoxin is responsible for the pathogenic action. An exhaustive study of this endotoxin has been made by Gallut and his associates. They found that a suspension of cholera vibrios in Ramon's broth medium, incubated at 37°C, began to develop toxin after 3 hours and attained a maximum potency after 4 hours. By this time, the pH had fallen to 5.8 and 99.5% of the vibrios were dead. After removal of the vibrios by centrifugation, a fluid was obtained, 0.05 ml of which was lethal for a 15-g mouse upon intraperitoneal administration. A still more potent toxin could be obtained by restoring the glucose content and pH of the centrifugate to the original values (5 g per litre and 8.0, respectively), adding a fresh culture of vibrios, and again incubating for 4 hours. With 5-10 repetitions of this process, the potency was increased about 5 times.

The toxin was subsequently shown to consist of two components, a glucolipoid having antigenic properties and a substance of smaller particle size, able to pass the ultrafilters. The glucolipoid produced congestion, whereas the other substance caused hypothermia. The latter substance was at first thought to be of a proteid nature, but later studies showed this to be unlikely. It was found to be non-precipitable by trichloracetic acid or by sodium tungstate, to be thermolabile, and not to possess antigenic power. Other workers have isolated what appear to be slightly different fractions, but Pollitzer is of the opinion that the cholera endotoxin is a single substance and somewhat labile, undergoing alterations during extraction and purification.

Another finding of considerable importance made by Gallut is that vibrios isolated from cholera patients vary in toxicity depending upon the stage of the disease. Maximum toxicity was found, on the average, 60 hours after the onset of the attack.

Some early workers considered the virulence of cholera vibrios to be merely a function of their toxicity. Dungern showed in 1895, however, that a freshly isolated, highly virulent strain and an old, almost avirulent stock culture had practically identical toxicities. The difference in virulence must therefore have been due to the greater viability of the freshly isolated strain, which was able to multiply rapidly in the peritoneal cavity of the experimental animals. Further studies have confirmed that the rate of multiplication of the organisms in the body is the most important determinant of virulence. As already discussed, however, subculture may lead to a change from the smooth to the rough form with loss of virulence due to qualitative changes. It is interesting to note that the virulence can be restored, or even enhanced, by repeated passage through intraperitoneally infected guinea-pigs. Studies by Husain & Burrows (1956) have further shown that strains of *V. cholerae* isolated from fatal and from non-fatal cases of cholera may be of equal virulence when tested in mice, so that, as these authors conclude, " the mouse LD_{50} criterion of virulence is, in fact, quite irrelevant to cholera in man ".

Immunity to cholera infection

It is well known that infection with cholera vibrios is by no means invariably followed by clinical manifestations of the disease. Most of the evidence indicates, however, that the defence mechanism is a non-specific resistance rather than a specific natural immunity. It has already been pointed out that the acidity of the stomach tends to destroy the vibrios, and there is also experimental evidence that a normal intestinal mucosa inhibits multiplication of the organisms, which have, in any case, to compete with the bacterial flora normally present. It is well established that persons suffering from chronic gastritis due to habitual alcoholic abuse are particularly susceptible to cholera and that temporary gastro-intestinal upsets favour cholera infection. Whether a specific natural immunity also exists seems doubtful, since it is impossible to demonstrate any significant titre of immune bodies in the sera of normal, non-vaccinated subjects.

Although second attacks have occasionally been observed after intervals of only a few weeks, there seems to be reason to believe that in general recovery from cholera confers at least a temporary immunity. It would be highly desirable to conduct large-scale studies in endemic areas to determine whether the inhabitants do acquire an immunity from slight and unrecognized attacks.

Whatever may be the truth in regard to naturally acquired immunity, there can be no doubt that an immunity of several months' duration can be actively induced by the administration of vaccines prepared either from living or from killed cholera vibrios. Although estimates of the duration of the immunity vary, most observations suggest that it is not less than 6 months and possibly as long as a year. Attempts at active immunization were made by Haffkine in 1892 using two live vaccines of different strength, according to the scheme adopted by Pasteur for rabies prevention. The difficulties of this method proved insuperable, however, for large-scale application. It had already been shown by Gamaleia in 1888 that guinea-pigs could be protected against lethal doses of *V. cholerae* by administering killed cultures, and in 1896 Kolle demonstrated the efficacy of this method in man. Furthermore, he was able to show that the bactericidal titres of the sera derived from persons who had received one injection of the killed vaccine were as high as or even higher than those of persons vaccinated three times by Haffkine's method. This is in accordance with the view now held that the immunizing effect is due to antigenic substances released from the bodies of the vibrios.

In the past, cholera vaccines have varied greatly in potency, and they are still prepared by a great variety of methods, using different strains, different culture media, and different methods of killing and preservation. In 1947, during the cholera epidemic in Egypt, the health authorities were confronted with a difficult problem because the vaccines supplied with the assistance of WHO varied in potency according to the country of origin. In the course of its work on the standardization of biological substances, WHO has given frequent attention to the problem of cholera vaccines and, as noted above, in 1954 an Expert Committee on Biological Standardization established International Reference Preparations of Cholera Antigen (Ogawa) and Cholera Antigen (Inaba).[4] In 1958, a Study Group was set up " to draw up requirements which should be fulfilled by preparations of yellow fever vaccine and cholera vaccine in order to ensure that these products are safe, reliable and potent prophylactic agents ".[5] In drafting the requirements for cholera vaccine, the Study Group found it necessary to leave many detailed specifications to be decided by national control laboratories, depending upon the methods used in the manufacturing establishments of the countries concerned. It was possible, nevertheless, to lay down certain guiding principles and to define a number of properties that should be found in all satisfactory vaccines. Provisional potency tests were also suggested. The Expert Committee on Biological Standardization

[4] *Wld Hlth Org. techn. Rep. Ser.*, 1954, **86**, 7.
[5] *Wld Hlth Org. techn. Rep. Ser.*, 1959, **179**.

subsequently requested the Statens Serum-institut, Copenhagen, to arrange a collaborative study of these potency tests, and it also supported the suggestion made by the Study Group that a well-controlled field trial of different batches of cholera vaccine should be carried out, including the International Reference Preparations. In this way, it is hoped to obtain international reference preparations of proven prophylactic efficacy.

In conclusion, mention may be made of some attempts to develop an antitoxic serum against cholera. In 1892, several workers reported that guinea-pigs could be protected against lethal doses of *V. cholerae* by intraperitoneal administration of milk from cholera-immunized goats, or of serum from persons vaccinated with live or killed cholera vibrios. Even very high doses of cholera convalescent serum were found inadequate, however, to save the lives of guinea-pigs already suffering from cholera. Various other methods were described for producing what were claimed to be antitoxic sera, sometimes using El Tor and other strains as well as *V. cholerae*. Pfeiffer and his associates were able to show, however, that the action of these sera is due to the presence of bacteriolysins and that they do not exert a true antitoxic effect. At the same time, they found that both immune serum and normal serum increased the tolerance of guinea-pigs to injections of toxin from killed cholera vibrios, and they attributed this to a non-specific action retarding the absorption of the toxin. On the other hand, Carrière & Tomarkin published in 1910 an exhaustive study of sera prepared from goats, horses, and rabbits, on the basis of which they concluded that it is possible to prepare cholera antitoxins, provided that the immunizing procedure is sufficiently prolonged. The best results were obtained by mixing the sera of different species of animals, immunized by various methods. These sera were innocuous when given to cholera patients, but large amounts were needed to assure therapeutic success. As Pollitzer concludes, however, " one should not lose sight of the fact that all cholera sera produced thus far exhibited but feeble anti-endotoxic properties, if any at all ", and it is therefore not surprising that attempts to treat cholera patients with immune sera have been abandoned.

The stray dog and rabies control

" Vaccination procedures will not reach the stray or ownerless dog, which remains a potential threat in the transmission of rabies in many countries. An efficiently conducted programme requires the operation of a local pound or humane animal shelter where stray animals may be kept for a few days and, if unclaimed at the end of that period, destroyed humanely. The practice of making stray impounded animals available for adoption as pets should be suspended during outbreaks of rabies in a community. Collection of strays should be carried out by teams of dog wardens and assistants in properly equipped trucks. Personnel responsible for this activity should be properly qualified and in-service training courses should be offered to them in such subjects as care and management, basic principles of animal disease control, first-aid, etc. Licensing or registration of all dogs is often a valuable adjunct. If properly enforced, it separates out the ownerless strays, helps to defray the expense of control activities and may serve as the basis for a reasonably accurate dog census."

From the fourth report of the WHO Expert Committee on Rabies (*Wld Hlth Org. techn. Rep. Ser.*, 1960, 201)

SECOND AFRICAN CONFERENCE ON BILHARZIASIS

With the development of irrigation systems, the prevalence of bilharziasis has increased in many countries. Thus, particularly in Africa, this disease presents a growing threat. During the last ten years or so, WHO has repeatedly warned the governments and other bodies concerned of the dangers of irrigation works that do not comply with the recommendations of the public health authorities.

Experts from several African countries and territories who participated in a Conference held at Lourenço Marques (Mozambique) from 30 March to 8 April 1960, under the auspices of WHO and of the Commission for Technical Co-operation in Africa South of the Sahara (CCTA), discussed various aspects of bilharziasis control in Africa, namely, prevalence and evaluation methods, diagnostic techniques, snail control, the use and development of water resources in accordance with public health requirements, agricultural techniques, and co-ordination of efforts, while bearing in mind that " the pressing problems of control are related rather to the deployment of skills, materials and work than to uncertainty of methods ".

The report of this Second African Conference on Bilharziasis which has just appeared [1] is briefly summarized below.

" Perhaps some small degree of bilharzial infection has been characteristic of the people of Africa for an immeasurable time but during the last half century or so it has become an increasingly prominent part of the African picture: it is an infection which development and progress have not only failed to control but have permitted, or perhaps encouraged, to increase far beyond its earlier prevalence." The Conference once more drew attention to this danger, and stressed the fact that means for the control of the disease are known but are not as widely applied as they should be.

[1] *Wld Hlth Org. techn. Rep. Ser.*, 1960, 204.

The medical and public health importance of bilharziasis

The report of the previous African Conference on Bilharziasis, held in 1956,[2] gave details on the distribution of the disease, which has hardly changed since then, although a large focus of *S. haematobium* infections has been discovered in northern Madagascar and another in the Republic of the Congo (Brazzaville). There has also been an increase in the frequency of human infection with schistosomes of the *S. bovis* group, particularly in certain irrigated areas where cattle are numerous. This infection has sometimes been found in as many as 40% of the inhabitants.

It is difficult to evaluate the morbidity and mortality attributable to schistosome infection, because such infection rarely appears in a well-defined, acute phase. Bilharziasis is essentially a chronic complaint with irreversible effects and sequelae, caused by the intense reaction around the eggs of the parasite. Three phases are distinguished in the evolution of the disease, namely, invasion, established infection, and irreversible effects and sequelae. Malnutrition, alcoholism, infectious hepatitis, pneumonia and tuberculosis are sometimes aggravating factors in bilharziasis. Cirrhosis and cancer of the liver as well as cancer of the bladder are considered to be frequent complications.

In *S. haematobium* infection the lungs are often involved in all of these phases. Adult worms may invade them and, though this is not generally known, eggs may sometimes be recognized in the sputum. It has been definitely established that this invasion may eventually lead to pulmonary hypertension, sometimes with cardiac failure. In areas where the disease affects children, it results in stunting of growth and endocrine disturbances.

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1957, 139.

The irreversible lesions and sequelae of bilharziasis are its most serious public health aspects, shortening the life of the individual and decreasing his ability to work.

The Conference formulated principles for the investigation of morbidity and the establishment of indices of prevalence. Diagnostic techniques based on the detection of eggs in the stools and urine are still important for survey purposes. Skin sensitivity tests, whose study and standardization are being encouraged by WHO, are promising. The same can be said of the fluorescent antibody technique in the serological study of bilharziasis, which gives hope of a more quantitative and precise understanding of human reaction and immunity to infection.

Snail control by chemical products

In reviewing the molluscicides applicable in Africa, the Conference pointed out their advantages and drawbacks and mentioned some new products, i.e., Bayer 73, ICI 24223 and Aqualin, which have been tried out on a small scale and would appear to be effective. It was found regrettable that only a small number of countries have undertaken large-scale snail control programmes. Molluscicidal measures could be taken in some territories even before the epidemiology of bilharziasis has been elucidated.

Economic development and spread of bilharziasis

The exploitation of water resources in Africa for economic development, and the construction of dams and irrigation systems multiply the number of suitable breeding places for invertebrates that transmit disease to man. The Conference noted the almost complete absence of regulations concerning the control of water in rural areas of Africa South of the Sahara. Its report cites some articles of an ordinance passed in the Belgian Congo in 1959 and advises the adaptation of legislative measures of this type to the conditions peculiar to each country. It also recommends the setting up of co-ordination committees within the framework of national organizations so as to ensure the fullest possible collaboration between all bodies participating in the development of water resources.

It is often necessary to make changes in the planning and construction of the facilities for water conservation and its use. Of course, it will not be possible to eliminate all the snail colonies in this way but those which remain can be controlled with molluscicides.

It would appear desirable to adopt new agricultural techniques, as has been done for rice-growing on an experimental farm in Ghana. These methods include: drilling the seed into dry soil, irrigating only long enough to obtain germination, turning water off for about four weeks, irrigating again until the rice ripens, and allowing the fields to dry out for harvesting. This system of intermittent irrigation appears to upset the snail and parasite cycles.

Engineering and agricultural features to be studied should include the following: types of practical canal lining and regulating structures; measurement of weirs; water velocities; the use of conduits and siphons; the possible use of water rotation systems to control snail and parasite cycles; and correlation of the modified rotation patterns with agricultural methods. Studies have shown that drainage and stream channelling will not only reduce or eliminate snail colonies, but will also make it possible to raise crops on formerly useless land.

The dominant question is whether the water supply is running or stagnant. In many parts of Africa there is no groundwater, or, if there is, it is not potable, so that the people are obliged to use surface water, which is sometimes very polluted and also often serves as a habitat for snails. Clearly, such sources of domestic water cannot be eliminated until other sources have been found. In certain cases rainwater—so far only inadequately collected—could make a valuable contribution. For example, it has been calculated that the roof area of a health centre in Togo could collect eight times the amount of the annual water ration now hauled by truck from a nearby reservoir. This estimate allows for a 60% loss of the annual rainfall.

It should also not be forgotten that washing and bathing places need to be provided in sites that are either healthy or involve less risk of contamination. Bridges and culverts over streams and canals must also be constructed, care being taken not to create breeding places adjacent to them. The value of these measures will be increased if they are accompanied by a programme of health education on the dangers of natural waters.

FIELD STUDIES AND TYPHOID VACCINES

The nineteenth century developed a system of dealing with communicable diseases that depended essentially on notification, isolation, and quarantine. Under this system a patient could theoretically be given suitable treatment, and the disease could be prevented from spreading to contacts. The system produced a remarkable drop in mortality rates in the second half of the century and at the beginning of the present century; but susceptible contacts often became infected before the patient was isolated, and during wars infection tended to spread like wildfire among the troops. Clearly some other method of protecting susceptible contacts was needed. The method sought was vaccination, which had proved so valuable in the control of smallpox.

Typhoid fever is a good example of such partially controlled diseases. No longer a scourge in Europe since its connexion with bad sanitation had been recognized and the appropriate sanitary measures taken, it still exacted a heavy toll in army camps. In England, Almroth Wright, who went as professor of pathology to the Army Medical School at Netley in 1892, developed from 1895 on a method of active immunization against typhoid fever, not by the Pasteur type of attenuated live vaccines, but by killed vaccines, and urged its adoption for active immunization of the army overseas. At first rejected by the War Office, his vaccine was later adopted, and as a result active immunization became a standard procedure in the British army. The low incidence of typhoid fever in this army during the First World War was largely attributed to active immunization with typhoid vaccine. Wright was not the first to develop such a vaccine nor was the British army the first to use mass vaccination; a typhoid vaccine had been developed by Pfeiffer & Kolle [1] in Germany and mass vaccination had been practised in the Russian army by Vysakovich.

Why was active immunization adopted in the United Kingdom after having originally been rejected? Part of the reason lies in the strong character of Wright, and part in the field studies of the Antityphoid Committee of the British Army Council, which carried out an extensive investigation with typhoid vaccines.[2] Between 1904 and 1908 specially appointed medical officers were attached to all army units leaving for Egypt or India, and instructed to inoculate all volunteers, keep records of those inoculated and those not, and note down all cases of typhoid fever in each group. The results were regarded as proving conclusively the value of vaccination against typhoid fever.

Clearly the evidence in favour of vaccination was regarded as adequate by the scientific standards of the day. Would it stand up to criticism now, more than fifty years later? The present view is that it would not.[3] The British Army Council trials were defective on many counts. To begin with, fresh batches of vaccine were often prepared, and then re-sterilized at each army station by heating to 60°C; thus the vaccine used was not of uniform quality. Then, sometimes only one dose of vaccine was given, sometimes two. The recording of the injections was unsatisfactory, the investigator having to depend on the soldier's statement. The diagnosis was often in doubt, no clear distinction being made between typhoid and paratyphoid fevers. More-

[1] Pfeiffer, R. & Kolle, W. (1896) *Dtsch. med. Wschr.*, **22**, 735.
[2] Cockburn, W. C. (1955) *Bull. Wld Hlth Org.*, **13**, 395.
[3] Cockburn, W. C. (1955) *J. roy. Army med. Cps*, **101**, 171.

over, it was frequently based on serological tests, whose results are still difficult to interpret. The incidence of infection was compared between those who volunteered for vaccination and those who did not: a comparison that nowadays is regarded as invalid on the ground that the very fact of volunteering creates a difference between the two groups. Men were transferred between units during the period of the study and inoculated at various times, some at the beginning, some at the end. Finally, the observers believed that the vaccine was of value, and may therefore have been biased when establishing a diagnosis.

At a European Seminar on the Application of Epidemiology in Health Administration, recently held by the WHO Regional Office for Europe at Opatija, Yugoslavia, one of the participants [4] made other criticisms of similar trials, carried out before the strict present-day criteria for controlled field trials were laid down or put into practice. Control groups were composed of persons who refused to be vaccinated and who were different in age and in other respects from those vaccinated. The system of recording was unreliable. The diagnosis was made largely on clinical grounds. Sometimes the number of observed cases was too small to allow of a sound conclusion. When persons were moved from the uninoculated to the inoculated group it was done with no knowledge of the problems of interpretation to which this gives rise.

Nevertheless, as a result of the field trials carried out fifty years or more ago, typhoid vaccines came into common use, and were soon followed by TAB (typhoid, paratyphoid A and paratyphoid B) vaccines. No strictly controlled field trial was ever made of these vaccines, which, since the trials, were tested only in laboratory animals or by measuring the agglutinin response in man. Numerous reports from laboratories have appeared describing large-scale observations on the value of alcoholized and phenolized typhoid vaccines, but without settling the important question which was the more effective in man. In 1953, therefore, WHO sponsored a study of the effectiveness of antityphoid vaccines in the prevention of typhoid fever. The Yugoslav Typhoid Commission [5] assisted by grants and expert advice from WHO and the US National Institutes of Health, organized in 1954 and 1955 a strictly controlled field trial of typhoid vaccines on the lines of those carried out on pertussis by the Medical Research Council of Great Britain.[6] The value of this British trial was that it had not only settled the controversy about the effectiveness of the various types of pertussis vaccine, but had also made it possible to correlate the results of the vaccine in children with the results of laboratory tests in mice.

The Yugoslav trial of typhoid vaccines [7] was designed to answer three questions:

1. Are the two most widely used vaccines, the alcohol-killed, alcohol-preserved and the heat-killed, phenol-preserved, of any value in the prevention of typhoid fever?

2. If the answer is yes, which is the more effective?

3. How do the results of laboratory tests of potency compare with the actual results in the field?

Persons between the ages of 5 and 50 in the area of the trial who volunteered to be inoculated were selected, provided that they were fit and had no previous history of typhoid fever or of recent typhoid inoculation. They were allocated by random sampling to three groups, one of which received the alcoholized vaccine, another the phenolized, and the third a phenolized vaccine prepared from *Shigella flexneri*—it being hoped that the third group would give some information about the value of vaccination against dysentery. The typhoid vaccines were prepared from a single large pool of cultures of *Salmonella typhi* strains Ty 2a and Ty 2b, half of the batch being treated with alcohol, the other half inactivated by heat and then having phenol added. The dosage was determined for vaccines; each vaccine was

[4] Dr B. Cvjetanovic, Medical Officer, Endemo-Epidemic Diseases, WHO Headquarters.

[5] Yugoslav Typhoid Commission (1957) *Bull. Wld Hlth Org.*, **16**, 897.

[6] Great Britain, Medical Research Council (1951) *Brit. Med. J.*, **1**, 1463.

[7] See *Chron. Wld Hlth Org.*, 1956, **10**, 153.

indicated by two code letters, so that the vaccinators did not know which of the vaccines they were giving. The number of persons who received the full course in 1954 was 35 508. Serological investigations were carried out on 200 persons in each year of the trial. Passive mouse-protection, active mouse-protection (without mucin), and Vi, O and H antibody-formation tests were performed.

This field trial in Yugoslavia conformed to the requirements of a strictly controlled field trial. It demonstrated the value of the phenolized vaccine, which gave protection to about 70% of those vaccinated. It showed that the phenolized vaccine is more effective than the alcoholized vaccine—which does not necessarily mean that the same degree of protection could be achieved with another batch of the same alcoholized or phenolized vaccine in other circumstances. Phenolized vaccine it demonstrated to be easier to use in the field because it does not require refrigeration. The trial also showed that the results of tests in animals are not directly applicable to man. These tests, as well as the serological tests, had led earlier investigators to the conclusion that the alcoholized vaccine was superior to the phenolized vaccine—so that British workers had preferred it and the British army had used it for nearly two decades, mistakenly, it now appears.

The trial pointed the way to fresh investigations. Previously it had been believed that the Vi antigen conferred virulence on *S. typhi*, and one of the reasons why alcoholized vaccine was thought to be superior to phenolized vaccine was that it produced a higher titre of Vi antibodies in those vaccinated with it. The trial suggested that the Vi antibody may be less important in man than in the mouse, and made it clear that much more work, including tests in the field, is required to determine the protective antibody in typhoid fever, the most effective antigenic preparations, and the best method of using them.

WHO has sponsored other controlled trials of typhoid vaccines in the field. Two—in Yugoslavia and in British Guiana—were organized in 1960, and more than 100 000 people were vaccinated in accordance with the principles laid down for controlled field trials. In these two trials, which have an identical programme, heat-killed, phenol-preserved dried typhoid vaccine and acetone dry typhoid vaccine have been used to determine which is the more effective.

Meanwhile, 18 laboratories all over the world interested in the laboratory testing and potency of vaccines have been taking part in the co-operative study of typhoid vaccines organized by WHO. The aim of the two field trials sponsored in 1960 is not only to determine the relative effectiveness of the two vaccines but also to correlate laboratory results with field results. Another field trial is being organized in Poland with types of vaccine as yet untested in the field, and will be linked with the trials in Yugoslavia and British Guiana.

By sponsoring these controlled field trials to assess the effectiveness of typhoid vaccines in man and organizing laboratory studies, WHO has initiated an international programme of research that will, it is hoped, lead to the establishment of standard typhoid vaccines and standard procedures for testing them, at the same time showing which is most effective in the control of typhoid fever. Although this disease is not a major public health problem in most European or other developed countries, it continues to be one in vast areas of the world. For its effective control environmental sanitation is essential, but at times of emergency typhoid vaccines may be the only method available; hence the importance of the problems to which a solution is now being sought.

TREATMENT OF RINGWORM BY GRISEOFULVIN

"A new era in the therapy of many of the common mycotic infections of the human skin, hair and nails may be at hand with the discovery of the almost unbelievable therapeutic effectiveness of the oral antibiotic, griseofulvin."[1]

Tinea capitis (ringworm of the scalp) is a dermatomycosis mainly affecting groups of children of school age. Although not serious in itself, the disease is conspicuous, and affects the morale of the children, keeping them from school and from participation in normal childhood activities. Furthermore, the bacterial complications to which it may give rise are sometimes serious.

The disease is carried home from school or from a group of playmates, and a reservoir of infection is then established among adults. In some communities in Israel, the proportion of adults suffering from ringworm is higher among women than among men. On the other hand, according to certain authors,[2] in Moslem communities it is the men who maintain the disease and run the risk of serious infection, because of their custom of shaving their heads, which is frequently done without due attention to hygiene. The Moslem women, however, are protected by the care they give their hair (washing, application of henna).

Ringworm is particularly widespread in communities where life is organized round the family or the tribe or where people live together in crowded conditions.

It has been observed that some persons contract ringworm more easily than others exposed to the same risk and that the disease is more frequent among children suffering from protein deficiency. In the Belgian Congo, Vanbreuseghem [3] examined thousands of children and found that its prevalence varied between 5% and 40%. It was higher in areas where serious protein deficiency was known to be present and kwashiorkor was encountered. The same applied to cases treated in hospital: at Bukavu, 89% of children suffering from kwashiorkor were infected with ringworm. At present it is impossible to say whether this arises from a lack of vitamin A accompanying protein deficiency, a change in the sebaceous secretion of the scalp, or some abnormality of the skin or hair related to kwashiorkor and favouring the development of fungi.

In North Africa, in some parts of Central Africa, in the Eastern Mediterranean basin, in certain parts of the USA where there is a high percentage of negroes, and in various parts of eastern Europe ringworm may affect 30-40% of children. The health authorities of several countries have decided to attack this problem and WHO is giving assistance in this field to the Province of Syria, United Arab Republic, and to Tunisia. In Yugoslavia, where a systematic campaign against ringworm is under way, the Organization has assisted a demonstration project of mass griseofulvin treatment, directed by Professor E. I. Grin.

The dermatophytic fungi (*Trichophyton, Microsporum*) live and multiply at the expense of the keratin they digest; as a result, the growth of the hair is impaired and it falls out, leaving bald patches.

The treatment used until quite recently consisted in the desquamation of the parts affected so as to remove the diseased keratin, and the disinfection of the patches in order to prevent contamination of new-formed keratin. For this purpose, fungicidal ointments and pomades, and even X-ray therapy—which causes depilation—were employed. None of these methods gave reliable and permanent results. It was necessary to find a new treat-

[1] Sulzberger, M. B. & Baer, R. L. (1959) *Excerpta Med. (Amst.), Sect. XIII*, 13, 145.

[2] Cheveriat, A. et al. (1960) *Maroc. méd.*, 39, 74.

[3] Vanbreuseghem, R. (1957) *Trans. roy. Soc. trop. Med.*, 51, 373.

ment, acting internally instead of externally, that would enable the keratin-producing cells to resist the fungus, and continue to resist it after they had become keratinized.

The discovery of griseofulvin was to provide an antibiotic satisfying these requirements. Isolated in 1939 from *Penicillium griseofulvum*, then from several other penicillia, the antibiotic was identified chemically and used in horticulture against certain fungal plant pathogens. Its powerful fungistatic action attracted the attention of dermatologists and, starting in 1958, studies were made of its use in the treatment of certain human and animal dermatomycoses. Encouraging reports came from hospitals in different parts of the world. The antibiotic gave better results than any form of treatment previously applied. It was more active when administered orally than parenterally, was not found in the serum of treated subjects but, on the other hand, could be detected in their hair. Since it was not bacteriostatic, it had no action on the intestinal flora. In therapeutic doses it did not have any harmful or irreversible side effects. As a result of these outstanding properties it was decided to use it for mass treatment.

One of the most recent applications of griseofulvin for the systematic control of ringworm was undertaken by the Government of Israel in an Arab village. Ziprkowski et al. describe this campaign and its results in a recent number of the WHO Bulletin.[4]

Following the mass immigrations from highly endemic areas after 1948, ringworm, which had been almost unknown in Israel, suddenly developed into a public health problem again. The number of new cases reached 4000-6000 yearly. Centres for X-ray treatment and topical applications of fungicides were established in the country but proved insufficient, although the number of persons treated yearly reached 2500. The good results obtained elsewhere with griseofulvin encouraged the Israeli health authorities to adopt it for a mass campaign after confirming its effectiveness and harmlessness in a preliminary trial with a group of children and women hospitalized at Tel-Hashomer.

Those most seriously affected are children aged from 5 to 14 years. Although in most cases the condition clears up spontaneously at puberty, some victims bear the marks of the disease throughout their lives.

Trichophyton violaceum is the most widespread parasite; favus caused by *T. schoenleini* is also encountered. In the Arab village where the campaign was carried out there were 441 *T. violaceum* and 5 *T. schoenleini* cases. Griseofulvin was administered in single doses of 25-30 mg/kg of body weight per day. At the end of 3 weeks there was a marked improvement in most cases. After 8 weeks, 99% of the *T. violaceum* infections and 60% of the *T. schoenleini* infections were cured. All cases were cured after 10 weeks' treatment. No topical application of ointment was made. The side effects reported comprise nausea, headache, some cases of furunculosis and one of skin eruption. Some degree of leukopenia was noted, but no agranulocytosis; investigations in this connexion will, however, be continued. Twenty-five cured cases which were followed up for 2-6 months did not suffer any relapse.

[4] *Bull. Wld Hlth Org.*, 1960, **23**, 803.

Notes and News

Ligation in the treatment of tumours

In the WHO programme for the encouragement of medical research, one of the recommendations was that, for their better understanding and treatment, pathological processes analogous to those in man should be studied in animals. Among these pathological processes spontaneous tumours in domestic animals seemed to be a suitable subject for study. A group of experts on animal and human cancers that met in January 1960 under WHO auspices proposed that therapeutic methods applicable to these tumours should be studied in the dog and cat.

Permanent ligation of the principal nutrient arteries has long been known to retard the growth of tumours. A different method recently introduced, resulting in complete regression of the malignant tumours, consists of temporary occlusion of the entire blood supply to a restricted accessible area of the body within the limits to which it can be tolerated by the surrounding tissues. This specific, selective lethal action of temporary ligation on tumour tissue opens up new therapeutic possibilities for human beings with some kinds of cancer.

Allen et al., who have been producing a series of studies on this subject since 1938, describe in the WHO Bulletin [1] some of the results they have obtained in dogs with various kinds of spontaneous tumours. They ligated 49 tumours for periods varying from 4 to 11 hours. In 29 out of 41 benign tumours—lipomas, angiomas, adenomas and mixed mammary tumours—they succeeded in destroying the tumour with no adverse effects on normal tissue included in the ligated portion. Two cases of warts, 2 of fibromas, 6 mixed mammary tumours and 2 testicular tumours resisted treatment. Total necrosis was observed in the 8 malignant tumours of this series—5 adenocarcinomas, 1 squamous cell carcinoma, 1 reticulum cell carcinoma and 1 amelanotic melanoma.

The outstanding feature of this method is the destruction of tumour tissue by a bodily process without participation of any outside agent. The inflammatory response following temporary anoxia appears to be essential to the destruction of the tumour, but as yet its exact role has not been elucidated. The multiplication of bacteria in the necrosing tumour is regarded as a consequence rather than a cause of the regression and disappearance of the tumour. The time for observation was too limited (up to 7 months) to show whether recurrence can take place.

Two hypotheses can be advanced to explain the destruction of tumours after complete but temporary ligation: one, death of the cells as a direct result of anoxia; the other, indirect effect of ligation, whereby inflammation occurs as a defence reaction of the body. These two hypotheses can also be combined.

The observations on spontaneous tumours in the dog confirm those made in a few human cases. This method thus gives hope of an additional therapeutic weapon being available for certain tumours—either inoperable tumours or tumours whose excision would involve particularly great risks or fearful mutilation. Ligation could also increase the response of certain tumours to other forms of treatment. Finally, the method opens the way to new experimental approaches to the fundamental growth processes of tumours at the cellular level, and to the role of anoxia and inflammation. With these ends in view research will continue on animals and on selected human cases. Although in this study the authors limit themselves to the effects of ligation only, they suggest trials of combinations of chemotherapy or irradiation with ligation, to reduce ligation time and extend the possible benefits.

[1] Allen, F. M., Kaplan, M. M., Meranze, D. R. & Gradess, M. (1960) *Bull. Wld Hlth Org.*, **23**, 727.

Public health aspects of low birth weight

The problem of prematurity and low birth weight was examined by a WHO Expert Group in 1950. It recommended the use by all countries of the international definition of prematurity (a birth weight of 2500 g or less) adopted by the First World Health Assembly in 1948. This definition has been widely accepted and has contributed to greater uniformity of vital statistics. In some areas, however, its adoption resulted in the registration of unusually high percentages of low-weight babies. In many of these areas lower levels have been adopted for local use and for practical purposes, partly because of the difficulties of providing even the simplest form of special care for all babies classified as premature under the international definition, and also because some workers have been of the opinion that the majority of these low-weight babies in fact do well without such special care.

This situation was examined by a WHO Expert Committee on Maternal and Child Health that met in Geneva from 21 to 26 November 1960. The Committee reviewed ways and means of reducing the problem of low birth weight, different kinds of care programmes, and methods of determining for individual countries or population groups birth weight levels at which various types of care are required. Many factors that play a part in low birth weight are still not fully understood; the Committee therefore outlined some of the more important studies, field investigations, and research projects that should be undertaken.

The Expert Committee's report will be reviewed in the *WHO Chronicle* when it is published.

Complications of isoniazid treatment

While the introduction of isoniazid has greatly facilitated the treatment of tuberculosis, there are still a number of problems involved in its use. For example, if the drug is administered in relatively high doses to patients suffering from malnutrition, the complication of peripheral neuritis may arise.

A recent number of the WHO Bulletin contains an account of a study of the problem at the Madras Chemotherapy Centre, India,[1] where this complication was noted in 20 out of 338 patients, drawn from a poverty-stricken malnourished section of the community, who were allocated at random to four different treatment schedules. Nineteen of these 20 patients were in groups receiving 7.8-9.6 mg/kg body-weight of isoniazid daily, and 18 were classified as slow inactivators of isoniazid. The remaining patient was in a group receiving 3.9-5.5 mg/kg body-weight daily plus PAS (*p*-aminosalicylic acid). The neuritis appeared in 9 of the cases in the first four months of treatment. Three very mild cases improved spontaneously without any specific treatment or discontinuation of the isoniazid. Large doses of pyridoxine and the discontinuation of the isoniazid proved effective in the treatment of the complication; pyridoxine is expensive, however. There was evidence that a vitamin B complex preparation in a daily dose containing 6 mg of pyridoxine was also an effective treatment, despite the continuation of the isoniazid. The prophylactic value of this preparation is now under study.

Expert Committee on Health Statistics

The information obtained from mortality statistics and from the statistics routinely collected by public health services is inadequate for the expansion of health programmes or even, in many cases, for evaluating the results of these programmes. Special surveys to supplement existing data are therefore becoming more frequent. National health surveys have been organized in six countries and are being considered in others; in many countries national surveys on specific diseases (tuberculosis, trachoma, etc.) have been carried out. Numerous local health and morbidity surveys have been executed or are being planned.

The statistics obtained from these surveys are rarely comparable, since the methodology,

[1] Devadatta, S. et al. (1960) *Bull. Wld Hlth Org.*, **23**, 587.

definitions and classifications employed differ widely not only from country to country, but from survey to survey. The results of individual surveys are frequently unsatisfactory, because adequate statistical methods have not been applied.

A WHO Expert Committee on Health Statistics, which met in Geneva from 5 to 10 December 1960, reviewed the whole question of health surveys. The Committee first considered the general characteristics, potentialities and limitations of health and morbidity surveys, distinguishing three main types: interview surveys, health examination surveys, and surveys based on existing record systems. The scope of local health surveys, specific disease surveys, and surveys in less developed areas was considered. The Committee also reviewed the preparations for the next revision of the International Classification of Diseases.

An account of the Committee's work will appear in the *WHO Chronicle* when its report is published.

The epidemiology of mental disorders

A WHO inter-regional conference was held from 6 to 15 December 1960 at Naples to discuss techniques of conducting surveys on the epidemiology of mental disorders. The participants were drawn from Southern European and North African countries in the European and Eastern Mediterranean Regions.

The conference discussed three main topics. One was sample surveys of prevalence, with special reference to the census method and the relationship of general demographic factors to mental health conditions. Another was surveys based on hospital populations, special attention being paid to the problems of retrospective and prospective cohort studies and the possibility of using hospital populations for assessment of the results of treatment. The third was studies of social influences on psychiatric pathology, especially in relation to epidemiological problems of migrating populations and the validation of results by the investigation of appropriate control groups.

Requirements for schools of public health

Reviewing in 1958 the question of the foreign student and the post-graduate public health course, a WHO Expert Committee suggested *inter alia* that WHO study the present development of schools of public health and the degree to which they are meeting world needs for health personnel. It went on to recommend that, when the study had been completed, detailed proposed standards for the minimum requirements for schools of public health should be prepared and discussed at an appropriate meeting.

The study has now been completed, and a WHO Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel met in Geneva, from 12 to 17 December 1960, to discuss recommended requirements for schools of public health.

The report of this Committee will be reviewed in the *WHO Chronicle* when it is published.

Occupational health in the Western Pacific Region

A seminar on occupational health was held in Tokyo, from 17 to 29 October 1960, under the joint auspices of WHO, ILO, and the Japanese Government. Its main objectives were to define the basic principles and aims of occupational health services, to identify and consider the outstanding problems of occupational health in the Western Pacific Region, and to discuss research and training in, and the promotion of, occupational health.

Occupational health has been defined by ILO and WHO as " the adaptation of work to man and of each man to his job". It includes promotion of the physical, mental, and social well-being of workers in all occupations and the prevention of occupational diseases and accidents. In highly developed countries modern occupational health services have been shown to promote orderly social and technological growth, and the money spent on them has often proved an investment rather than an expense. Industrialization that ignores the human factor runs the risk of causing social upheaval, increased mental stress,

more accidents, and more occupational disease, and this risk may be obviated by the introduction of occupational health services *pari passu* with the introduction of new industries.

This seminar, the first ever to be organized on occupational health in the Western Pacific region, was attended by public health and labour department officials from countries and territories in the Region.

Diarrhoea and sanitation

The improvement in potable water supplies during the last years of the nineteenth century and the first years of the twentieth was followed by a marked decrease in the incidence of typhoid fever. Although no such definite correlation was noted in respect of diarrhoea morbidity and mortality, S. W. Simmons, writing in a recent number of the *Boletín* of the Pan American Sanitary Bureau, [1] observes that this type of disease becomes less frequent when the following improvements are introduced into a community: (1) an adequate water supply in each home; (2) a hygienic system of evacuating excreta; (3) elimination of soil contamination; (4) elimination of flies, and in some places of snails that are the hosts of *Schistosoma*; (5) provision of sufficient domestic living space; (6) exercise of adequate control over food hygiene. It is usually admitted that diarrhoea and dysentery, and in particular the bacillary forms of these diseases, tend to disappear when all these sanitary measures are adopted.

The supply of potable water is considered as a rule to be the first prerequisite for the prevention of diarrhoeal diseases. However, recent studies on shigellosis seem to indicate that the quantity of water available for personal hygiene is at least as important as, if not more important than, the quality of the water. Although outbreaks of water-borne shigellosis have been notified, investigations have shown that *Shigella* dies quickly in water, and very few epidemics can be specifically attributed to it. On the other hand, *Shigella* can be easily passed from one person to another—which means that personal hygiene is an important factor. It has been proved that there is considerably more shigellosis among families without laid-on water in their homes than among those who have this amenity, whereas no difference of incidence is noted as between communities with a municipal water supply and communities using well water liable to be contaminated. The rates observed in Kentucky among pre-school-age children are enlightening: 1.1% in localities with domestic water supplies and adequate facilities for the evacuation of excreta; 2.4% in localities with water laid on to the homes but with latrines outside; 5.9% in localities where both latrines and water points are outside; and 6% in localities where the water supply is at a distance. In the camps for immigrant workers in California, the rates for *Shigella* infection among children of families using outside latrines were approximately double those for families with inside latrines.

In tropical and sub-tropical countries, flies are among the main vectors of diarrhoeal diseases. In the low-lying region of the Rio Grande Valley, it was found that total elimination of flies reduced *Shigella* infection by approximately 40%. The best way of combating flies is, by environmental sanitation, to prevent their propagation. Any municipal sanitation programme must first and foremost include appropriate measures for the collection and disposal of refuse.

[1] Simmons, S. W. (1960) *Bol. ofic. sanit. panamer.*, **49**, 439.

WHO membership

The Gabon Republic and the Federation of Nigeria have become full Members of WHO by depositing with the Secretary-General of the United Nations formal instruments of acceptance of the WHO Constitution. This brings the number of States that are full Members of the Organization up to 100.

Both the Gabon Republic and the Federation of Nigeria were admitted to Associate Membership of WHO in May 1960. Since then they have acquired political independence, thus becoming eligible for full Membership.

Goitre in New Zealand

In an article on the world distribution of endemic goitre, which appeared in the September

1960 number of the *WHO Chronicle*, it was stated (p. 345) that in New Zealand " goitre is believed to have been prevalent among the Maoris long before the advent of the British settlers; it is now common both in North and South Island ".

Dr H. B. Turbott, Director-General of Health, New Zealand, points out that " goitre was not prevalent among the Maoris before the advent of the British settlers except for the tribes which lived in the inland high country. Those who lived near to the sea had a diet containing plenty of fish and sea foods which guarded them from this complaint." Dr Turbott adds that " goitre is now most uncommon in New Zealand. Since the introduction of iodized salt, goitre has been practically eliminated. The sale of iodized salt is not compulsory, but it is used nationally for table and culinary purposes."

People and Places

Improving midwifery services

A programme for the improvement of midwifery services in the Philippines was started, with help from WHO and UNICEF, in 1953. Hilots (traditional birth attendants) are trained in new methods of delivery and infant care. Regional centres train nurse-midwife supervisors, who in turn supervise and teach the hilots. Midwifery schools have improved public health nursing and midwifery practice.

The Government of the Philippines, WHO and UNICEF are now collaborating on an over-all evaluation of midwifery education and services in the Philippines. Plans are under way to establish advanced education programmes to prepare midwives for teaching and supervisory positions in the health services.

Miss Lalla Goggans, Regional Nursing Consultant, United States Children's Bureau, who is serving as a consultant on this programme for three months, has a Master's degree in administration and public health nursing from Teachers College, Columbia University. She has taken advanced courses in paediatric nursing and midwifery and has worked as a public health nurse and midwife and as a public health nurse supervisor.

Malaria field appointments

Professor G. A. Livadas has been appointed short-term consultant to the WHO-assisted malaria eradication programme in Madagascar, where his wide experience as an epidemiologist will be of value in the preparation of a detailed plan for surveillance in the High Plateau. He will spend several months studying the health services in each sector and the use to be made of them in case-detection operations, which will involve a population of about two million. Professor Livadas is a distinguished Greek malariologist, and served as Chairman of the WHO Expert Committee on Malaria in 1956. He has acted as WHO malaria consultant in a number of countries, including India, Burma, Thailand, Indonesia, Afghanistan, Lebanon, the United Arab Republic (Province of Syria) and Jordan, and he recently organized surveillance activities in the South Cameroun pilot zone.

Professor Giuseppe Saccà has been appointed scientist (entomologist) in the malaria eradication programme in Jordan. This programme, in which—in addition to residual spraying—there is a good deal of larviciding as a counter-measure against the elusive habits of *Anopheles sergenti*, the main vector, has been assisted by UNICEF, the United Nations Relief and Works Agency (UNRWA) and the United States International Co-operation Administration (ICA), as well as by WHO. A feature of the entomological situation is the resistance of *A. sergenti* to dieldrin in certain areas of the Jordan Valley; on the other hand another vector, *A. sacharovi*, is reported to have disappeared as a result of DDT spraying. WHO continues to stress the importance of the entomologist in malaria eradication programmes, not only in planning but also in the attack and consolidation phases. Professor Saccà has for many years been medical entomologist on the staff of the Istituto Superiore di Sanità in Rome.

He has already worked for WHO as short-term consultant in the pre-eradication malaria survey concluded in Morocco in October 1959.

BCG vaccination studies

The Government of French Polynesia has asked for WHO help in providing mass BCG vaccination for the population below 20 years of age. The vaccination programme will be combined with a study of the immunological relationship between tuberculosis and leprosy, and later with the development of tuberculosis control, including institutional treatment and ambulatory chemotherapy, for the territory. As part of its assistance, WHO is providing a consultant to survey the situation and make recommendations for a future programme.

The consultant chosen for this task is Dr Hillel Beham, Chief of the Tuberculous Children's Department at the Eitanim Hospital, Jerusalem. After medical training in Jerusalem, Lyons, New York and Paris, Dr Beham has worked in East Africa and held various posts in the Ministry of Health of Israel.

Medical instruction in Cambodia

Since 1953, WHO has been helping the Royal School of Medicine, Phnom-Penh, Cambodia, to raise its standard of teaching to professional level. As part of this programme, Dr Hubert Loncin was recently appointed to teach physiology at the School. Of Belgian nationality, Dr Loncin has worked at the Institute of Physiology of the Université libre de Bruxelles.

Study on traffic accidents

Dr Leslie G. Norman, of the United Kingdom, has been appointed by WHO to prepare a report on road traffic accidents, with special reference to epidemiology, causative factors and prevention.

Dr Norman is Chief Medical Officer of the London Transport Executive. He studied at University College Hospital Medical School, London, and is a member of the WHO Expert Advisory Panel on Occupational Health. In 1952 and 1953 he represented WHO at a meeting of the Working Party on the Prevention of Road Traffic Accidents of the Economic Commission for Europe Inland Transport Committee, and its subgroup meeting on Physiological and Mental Standards for Drivers. In 1955 he was a member of the Consultant Group on Medical Requirements for the Licensing of Motor Vehicle Drivers convened by WHO.

Diarrhoeal Diseases Advisory Team

Dr W. J. van Zijl of Leiden, Netherlands, has been appointed epidemiologist on the WHO Diarrhoeal Diseases Advisory Team. A graduate of the Veterinary and Medical Schools of Utrecht University, Dr van Zijl is a specialist in bacteriology and holds diplomas in public health and in tropical medicine and hygiene from the University of Leiden. He has had extensive training and experience in microbiology and parasitology.

Dr van Zijl will be leader of the team, which includes a bacteriologist—Dr Nina Blioumel, of the USSR [1]—in a permanent capacity, as well as a paediatrician-nutritionist and a sanitary engineer on a short-term basis. In 1961, the team will visit several Member States of WHO where diarrhoeal diseases are an important public health problem, and will help the health authorities evaluate the situation and establish effective control programmes.

Vaccine production in India

Dr Abel Tasman has been assigned by WHO to help the Central Research Institute, Kasauli, India, start production of diphtheria, pertussis and tetanus vaccines. Though he will spend only six weeks at the Institute, he will continue to advise it during the initial period of production.

Dr Tasman has, for many years, been at the head of the laboratory for the purification of sera and vaccines at the State Institute of Public Health, Utrecht, Netherlands. He has on several occasions helped with similar WHO/UNICEF-assisted projects for the production of sera and vaccines used in the prevention of infectious childhood diseases.

Health work among Arab refugees

Dr Jean Puyet was recently appointed epidemiologist on the WHO staff seconded to the United Nations Relief and Works Agency (UNRWA), whose health division is in Beirut, Lebanon. His main task will be to plan and carry out epidemiological surveys and com-

[1] See *WHO Chronicle*, 1960, **14**, 241.

municable disease programmes among Palestine Arab refugees in Jordan, Gaza, Lebanon and the United Arab Republic (Province of Syria).

After qualifying in medicine in Paris, Dr Puyet took a Master's degree in public health administration and tropical medicine at Harvard University. He has served with the International Refugee Organization and with UNRWA, for which he undertook retrospective and concurrent epidemiological analyses of cases of infant morbidity and mortality in certain camps in Lebanon.

Nursing education in Jamaica

Miss Kathleen Durrell of Winnipeg, Canada, has been appointed by the Pan American Sanitary Bureau, which acts as the WHO Regional Office for the Americas, as nursing education consultant to the Government of Jamaica. In this capacity, she will advise the appropriate authorities on the development of modern programmes of nursing education at the basic and post-graduate levels.

Miss Durrell received her B.S. degree in nursing from the University of Alberta, Edmonton. She also holds a Master's degree in nursing administration and education from the University of Washington and teaching qualifications from McGill University, Montreal. After serving as Director of Nursing Education at the Winnipeg General Hospital, and as Medical Clinical Supervisor at University Hospital, Edmonton, Miss Durrell joined the staff of WHO in 1953 to work as a nursing educator in India. From 1957 until her present appointment, she was a WHO nursing instructor in Iran.

Clinical pathology consultant for Malaya

Dr Regino J. Navarro, Professor of Medicine and former Head of the Clinical Laboratory, University of the Philippines and Philippine General Hospital, has been appointed WHO consultant in clinical pathology at the Institute for Medical Research, Kuala Lumpur, Federation of Malaya.

Dr Navarro obtained his medical degree from the University of Illinois and his B.Sc. degree from the University of the Philippines. After working as assistant bacteriologist at the Bureau of Science in Manila and as a serologist at Columbus University, Chicago, Ill., he joined the medical faculty of the University of the Philippines as Assistant Professor in Pathology and Bacteriology, becoming Professor of Medicine in 1940.

Public health adviser to Nepal

Dr M. L. Ahuja, well-known Indian bacteriologist and former Director of the Central Research Institute, Kasauli, and the Pasteur Institute, Coonoor, has been appointed WHO public health adviser to the Government of Nepal. One of his principal tasks will be to help the Government in assessing the country's medical and health needs, and in streamlining the administrative machinery to ensure the effective guidance and supervision of public health activities. As WHO representative in Nepal, he will also help to co-ordinate all assistance in the field of health received by the country from external sources and will advise the WHO Regional Office for South-East Asia on the planning and development of WHO-assisted health projects in Nepal.

Dr Ahuja has been a member of the WHO Expert Advisory Panels on Biological Standardization and Rabies, and has undertaken a number of assignments for the Organization.

Problems of air pollution

Dr August T. Rossano, of the United States, was recently appointed by WHO to undertake a study of air pollution problems, with a view to the world-wide standardization of nomenclature and instrumentation in this field. In the course of this assignment, he visited some of the air pollution experts and centres in a number of European countries.

Dr Rossano is a civil engineering graduate of Massachusetts Institute of Technology, and holds a doctorate in science from Harvard University. Specializing first in industrial hygiene, he directed programmes in this field for the state health departments of Washington, California, Colorado and Alabama. In 1955 he was put in charge of field studies at the Robert A. Taft Sanitary Engineering Center, Cincinnati, Ohio, and worked in the Center's air pollution research programme until 1959 when he was appointed Visiting Professor in Air Pollution and Radiological Health at the California Institute of Technology.

Review of WHO Publications

BIOLOGICAL SUBSTANCES

Study Group on General Requirements for the Sterility of Biological Substances: Report (World Health Organization Technical Report Series, No. 200), Geneva, 1960, 31 pages. Price: 1/9, $0.30, or Sw. fr. 1.—.

This report is the fourth in a series containing requirements for biological substances recommended by WHO study groups for international adoption. The earlier reports contained general requirements for manufacturing establishments and control laboratories and requirements for four specific vaccines.[1] Inevitably, these included sections on sterility tests, but the aim of the present report is to formulate requirements applicable to all important biological preparations for which sterility is imperative. For inactivated and live virus vaccines, it is usual to design specific tests to detect viral contaminants. In view of its growing importance, however, the Study Group [2] also attempted to formulate some recommendations of a general nature concerning this aspect of sterility control.

Like its predecessors, the report is divided into two parts, the first consisting of a summary of the general considerations of the group and recommendations for further studies, while the second contains the requirements proper. These are set out according to the same pattern as the previous requirements, with explanatory or amplifying notes added in small type. The presentation is such that if the requirements are found by national authorities to be appropriate to their needs they can be used as they stand as definitive national requirements. An appendix to the requirements contains the formulae and methods of preparation of a number of media currently used for sterility tests in various control laboratories.

[1] *Wld Hlth Org. techn. Rep. Ser.*, 1960, 178, 179, 180; see also *WHO Chronicle*, 1960, 14, 78.

[2] Members of the Study Group: Dr M. Weis Bentzon, Denmark; Dr P. H. Bonnel, France (Rapporteur); Dr P. de Góes, Brazil; Dr M. Pittman, USA (Chairman); Dr G. Penso, Italy; Dr R. H. Regamey, Switzerland; Dr Sumiatno, Indonesia (Vice-Chairman); Dr J. O'H. Tobin, United Kingdom (Rapporteur); Dr G. V. Vygodchikov, USSR. Secretariat: Dr B. K. Bhattacharya, WHO; Dr N. K. Jerne, WHO (Secretary).

MALARIA ERADICATION

Expert Committee on Malaria: Eighth Report (World Health Organization Technical Report Series, No. 205), Geneva, 1961, 50 pages. Price: 3/6, $0.60, or Sw. fr. 2.—.

Although progress towards world-wide malaria eradication has, in general, been very satisfactory, some eradication programmes have failed to develop as speedily as they should. The eighth report of the WHO Expert Committee on Malaria [1] is mainly concerned with the reasons for these failures and with methods of increasing the efficiency of eradication programmes. The technical, operational and administrative causes of failure are analysed in detail and it is emphasized that success depends not only on careful planning and meticulous execution of the programme, but also on the full support of the national authorities at every stage. This must be ensured at the outset by a signed undertaking from the government.

The criteria given in the Committee's seventh report for discontinuing spraying operations and starting the consolidation phase are amplified and a fresh criterion added, namely, that surveillance should be fully established and adequate. The measures undertaken should include the passive as well as the active detection of cases, this being the only way to ensure that all areas

[1] Members of the Committee: Col. M. K. Afridi, Pakistan (Chairman); Professor G. D. Belios, Greece (Rapporteur); Dr Wan-I Ch'en, China (Taiwan); Dr G. R. Coatney, USA (Chairman); Professor S. Farman-Farmaian, Iran; Dr M. B. Marquez-Escobedo, Mexico; Professor G. Macdonald, United Kingdom; Dr A. P. Ray, India; Dr B. Richter, Yugoslavia; Professor P. Serguiev, USSR. Secretariat: Dr C. A. Alvarado, WHO; Dr L. J. Bruce-Chwatt, WHO; Dr A. Gabaldón, Venezuela (Consultant); Professor P. C. C. Garnham, United Kingdom (Consultant); Professor E. J. Pampana, Italy (Consultant); Dr E. B. Weeks, WHO (Secretary); Dr P. Yekutiel, WHO; Dr R. W. Fay, WHO; Mr J. W. Wright, WHO.

are reached and observations are continuous. With a view to reducing the costs of the consolidation phase without sacrificing efficiency, the report recommends that WHO should study the costs by heads of expenditure in as many countries as possible, and should encourage the detailed analysis of costs both by activity and by heads of expenditure in selected representative countries.

The report reaffirms that eradication may be considered to have been achieved " when an adequate surveillance mechanism has not discovered any evidence of transmission or residual endemicity, despite careful search, during three consecutive years ". The criteria of eradication given in the sixth report of the Expert Committee on Malaria are re-examined; while the basic principles remain unchanged, the criteria are redefined and expanded so as to cover the needs of special situations that have been met in practice. With the object of establishing an official register of areas where eradication has been achieved, recommendations are given on the methodology of inspection and certification.

In countries where the administrative structure and the health services are still in the development stage, a " pre-eradication programme " may be necessary to create suitable conditions for the success of malaria eradication. An outline of such a programme is given and it is suggested that an international team should be provided to advise the government and, if necessary, to carry out the initial stages of the programme.

Health education forms an essential part of a malaria eradication programme; it must reach all levels of the population from the outset of the campaign and be continued throughout the consolidation and maintenance phases, in order to ensure the continued co-operation of the public at a time when interest in malaria will have begun to wane. The report advocates that provision should be made for a special staff to run health education programmes under the eradication programme.

The establishment of a standard terminology for use in evaluation and surveillance was considered by the Committee to be highly desirable, and it was recommended that WHO set up a drafting committee to undertake this task.

The report draws attention to the value of chemotherapy in the attack phase of eradication programmes as well as in the later phases. The 4-aminoquinolines remain the most effective drugs and no significant changes are recommended in the regimen for radical cure. The use of salt medicated with chloroquine shows promise. Research is needed on the improved use of available drugs and to discover compounds with an improved action against malaria parasites.

It is believed that in some countries a reduction in the standard dosage of DDT (1 g/m²) used for spraying might be possible, but no such reduction should be made until appropriate field trials have provided unequivocal evidence that this would not jeopardize the success of the eradication programme.

Finally, the report considers the relation of simian to human malaria, particularly the recent experimental transmission of malaria from the lower monkeys to man. For a variety of reasons, it is concluded, however, that the practical importance of a simian reservoir of malaria is likely to be small.

AIRCRAFT DISINSECTION

Aircraft Disinsection. Eleventh Report of the Expert Committee on Insecticides. (*World Health Organization Technical Report Series*, No. 206), Geneva, 1961, 26 pages. Price: 1/9, $0.30, Sw. fr. 1.—.

The accidental transportation of insects from one territory to another raises public health problems of considerable magnitude, since it could jeopardize the success of such programmes as the eradication of malaria and of the *Aëdes aegypti* mosquito. The consequences may be particularly disastrous if resistant strains of such insect vectors are introduced from one country into another. If all international airports complied with the requirements of the International Sanitary Regulations regarding the protection of airports from mosquito vectors, the risk of carriage of these insects by aircraft would be greatly reduced and insecticidal treatment, or " disinsection ", of aircraft would be relegated to a second line of defence. Unfortunately, the information available to the WHO Expert Committee on

Insecticides [1] did not indicate that this was the case; in fact, it revealed a generally disquieting state of affairs regarding the current status of vector control at a number of international airports. The Committee's report strongly urges that an effective vector control organization, under the auspices of the national health authority, should be set up at each international airport, and requests WHO to provide governments with such technical advice as may be needed.

The report notes that many countries still use in-the-air disinsection of aircraft with aerosols although this method has been proved to be ineffective. Post-arrival treatment causes undesirable delays and also allows opportunities for the insects to escape before application of the insecticide, while the method of pre-departure disinsection currently practised permits subsequent re-infestation. The report therefore recommends that disinsection should be performed after the passengers have embarked and the doors have been locked and immediately before take-off (" blocks away " disinsection). A procedure designed to make this method as effective as possible is recommended, but it is recognized that the use of aerosols inevitably has a number of disadvantages and limitations, which could be overcome by applying an insecticide in vapour form. A recently discovered derivative of dichlorovinyl phosphate (DDVP) appears to be very suitable for this purpose and a satisfactory mechanical system has been developed for its application. Vapour disinsection is a highly promising method since it is not only more effective than the aerosol method but can also be used for in-the-air disinsection and will therefore be more acceptable to health authorities. The report recommends that it should be universally adopted as soon as the necessary development work has been completed. A number of desirable improvements in the method and other recommendations for further research are outlined. Since aerosols are likely to continue in use for some time, a tentative method for the bioassay of candidate aerosols and test procedures for aerosols and aerosol dispensers are annexed to the report, as well as a list of aerosol formulations that have been found effective in practice.

[1] Members of the Committee: Mr R. W. Bonhoff, Germany; Dr R. A. E. Galley, United Kingdom; Dr Marshall Laird, Canada (Chairman); Dr J. Lembrez, France (Vice-Chairman); Dr R. Pal, India; Mr K. D. Quarterman, USA (Rapporteur). Representative of the International Civil Aviation Organization: Dr F. de Tavel. Secretariat: Dr P. Bertagna, WHO; Dr R. W. Fay, WHO; Dr M. J. Freyche, WHO; Mr J. W. Wright, WHO Secretary).

Second African Conference on Bilharziasis (WHO/CCTA): Report (*World Health Organization Technical Report Series*, No. 204), Geneva, 1960, 37 pages. Price: 1/9, $0.30, or Sw. fr. 1.— This report is discussed in the article on page 59.

Trends in Juvenile Delinquency, by T. C. N. Gibbens, World Health Organization, Geneva, 1961 (*Public Health Papers*, No. 5), 56 pages. Price: 3/6, $0.60 or Sw. fr. 2.—.

This publication is considered at length in the article on page 39.

BULLETIN

OF
THE WORLD HEALTH ORGANIZATION

DE
L'ORGANISATION MONDIALE DE LA SANTÉ

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Treatment of spontaneous tumours by temporary local ligation: a comparative study in dogs—*Frederick M. Allen, Martin M. Kaplan, David R. Meranze & Morton Gradess*

Some epidemiological aspects of the eradication of yaws—*C. J. Hackett*

The diarrhoeal diseases in England and Wales: with special reference to those caused by *Salmonella, Escherichia* and *Shigella—Joan Taylor*

Anaemia in Mauritius—*Gordon Stott*

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Medico-legal aspects of medical certification of cause of death—*Antti Isotalo*

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